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SEARCH REQUEST FORM

Scientific and Technical Information Center

Full Name: Geetha Bansal Examiner # : 73967 Date: 8/19/01

1642 Phone Number 305-3955 Serial Number: 09/529639

Mail Box and Bldg/Room Location: 8A03 CM1 8E12 Results Format Preferred (circle): PAPER DISK E-MAIL

If more than one search is submitted, please prioritize searches in order of need.

****

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: Tumor Vaccine

Inventors (please provide full names): Wagner, Ernst; Kircheis, Ralf; Grimmelin, ... DE 19746173 ... Schooten, ...

Earliest Priority Filing Date: 18 October 1997 (PCT/EP98/06546)

***For Sequence Searches Only* Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.**

Please search the following claimed subject matter

1) Tumor vaccine comprising tumor ~~antigen~~ (tumor cells also) ~~delayed release system~~ for IFNγ, dose of IFN-γ is 50ng–5... release interval 30 minutes – 8 days.

2) Tumor vaccine comprising tumor antigen and IFNγ at 100ng – 2μg in a delayed release system (such as in liposomes or microspheres &) or mini pellets

3) as above wherein release interval is 30 minutes – 2 to 3 days

4) 75% of IFN dose is released in 1 hour – 3 days

5) liposomes wherein containing IFN-γ has 90% inside liposome 10% adsorbed to outside

Thank you

Vaccine pictured thus: ... vaccine = tumor cell + IFN liposome

****

STAFF USE ONLY	Type of Search	Vendors and cost where applicable
Searcher:	NA Sequence (#)	STN
Searcher Phone #:	AA Sequence (#)	Dialog
Searcher Location:	Structure (#)	Questel/Orbit
Date Searcher Picked Up: 8-23-01	Bibliographic ✓	Dr.Link
Date Completed: 8-30-01	Litigation	Lexis/Nexis
Searcher Prep & Review Time:	Fulltext	Sequence Systems
Clerical Prep Time:	Patent Family	WWW/Internet
Online Time: 70	Other	Other (specify)

PTO-1590 (1-2000)

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     (FILE 'HCAPLUS' ENTERED AT 09:40:41 ON 23 AUG 2001)
               DEL HIS Y
L1         11459 S TUMOR (L) (ANTIGEN#)
L2         25703 S GAMMA (L) (INTERFERON# OR IFN)
L3         34541 S VACCIN?
L4           985 S L1 AND L2 AND L2
L5           985 S L1 AND L2
L6           153 S L3 AND L5
L7         47764 S ANTITUMOR (L) AGENT#
L8           121 S L5 AND L7
L9           211 S L6 OR L8
L10        41392 S LIPOSOM? OR MICROSPHER? OR MINIPELLET# OR MICRO(L) SPHER?
OR
L11           20 S L9 AND L10
L12        16348 S (SLOW OR DELAY? OR TIME? OR CONTROLL? ) (L) RELEAS?
L13            2 S L11 AND L12
L14          131 S L2 (L) L10
L15           23 S L14 AND  L3
L16            4 S L15 AND L7
L17            6 S L16 OR L13
L18           18 S L11 NOT L17

=> d .ca l17 1-6;d ibib hitind l18 1-18


L17  ANSWER 1 OF 6  HCAPLUS  COPYRIGHT 2001 ACS
ACCESSION NUMBER:         2001:416792  HCAPLUS
DOCUMENT NUMBER:          135:10056
TITLE:                    Controlled delivery of antigens
INVENTOR(S):              Caplan, Michael; Burks, Wesley A., Jr.; Bannon, Gary
                          A.
PATENT ASSIGNEE(S):       The Board of Trustees of the University of Arkansas,
                          USA; Panacea Pharmaceuticals, LLC
SOURCE:                   PCT Int. Appl., 34 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.        KIND  DATE          APPLICATION NO.  DATE
     ---------------   ----  --------      ---------------  --------
     WO 2001039800      A2   20010607      WO 2000-US42607  20001206
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR,
             HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT,
             LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU,
             SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU,
             ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
             DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
             BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
PRIORITY APPLN. INFO.:                    US 1999-169330   P  19991206
AB   Formulations and methods are developed for delivering antigens to
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individuals in a manner that substantially reduces contact between the antigen and IgE receptors displayed on the surfaces of cells involved in mediating allergic responses, which target delivery of antigen to dendritic, phagocytic and antigen presenting cells (APCs), and which have improved pharmacokinetics. By reducing direct and indirect assocn. of antigens with antigen-specific IgE antibodies, the risk of an allergic reaction, possibly anaphylactic shock, is reduced or eliminated. Particularly preferred antigens are those that may elicit anaphylaxis in individuals, including food antigens, insect venom and rubber-related antigens. In the preferred embodiments, the compns. include one or more antigens in a delivery material such as a polymer, in the form of particles or a gel, or lipid vesicles or liposomes, any of which can be stabilized or targeted to enhance delivery. Preferably, the antigen is surrounded by the encapsulation material. Alternatively or addnl., the antigen is displayed on the surface of the encapsulation material. One result of encapsulating antigen is the redn. in assocn. with antigen-specific IgE antibodies. In some embodiments, antigens are stabilized or protected from degrdn. until the antigen can be recognized and endocytized by APCs which are involved in eliciting cellular and humoral immune responses. In a preferred embodiment, the formulation is designed to deliver antigens to individuals in a manner designed to promote a Th1-type mediated immune response and/or in a manner designed to

suppress a Th2 response. In still another embodiment, the formulation effects preferential release of the antigen within APCs. For example, various synthetic, biodegradable polymeric microsphere formulations were prepd. contg. peanut allergen. Microspheres based on poly(lactide-co-glycolide) (75:25) contg. an acid end group (0.1% loaded with allergen) had the lowest amt. (<20 ng) of peanut protein detected on the outside of the microsphere and the best range of peanut protein allergens contained within the microspheres (having mol. wts. ranging from 15 kDa to 70 kDa).

IC ICM A61K039-00

CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 15, 17

ST antigen **controlled release** lipid polymer encapsulation; immunomodulator immunoadjuvant antigen **controlled release**

IT Immunoglobulins
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(E; encapsulation of antigens for **controlled release** and immunomodulation)

IT Crosslinking
(IgE receptors; encapsulation of antigens for **controlled release** and immunomodulation)

IT Immunoglobulin receptors
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(IgE, crosslinking of; encapsulation of antigens for **controlled release** and immunomodulation)

IT Lymphocyte
(activation; encapsulation of antigens for **controlled release** and immunomodulation)

IT Immunostimulants
(adjuvants; encapsulation of antigens for **controlled release** and immunomodulation)

IT Peanut (Arachis hypogaea)
(allergens; encapsulation of antigens for **controlled release** and immunomodulation)

IT Food
(antigens; encapsulation of antigens for **controlled release** and immunomodulation)
IT Antigens
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(autoantigens; encapsulation of antigens for **controlled release** and immunomodulation)
IT Polymer degradation
(biochem., hydrolytic; encapsulation of antigens for **controlled release** and immunomodulation)
IT Interleukin 12
Interleukin 18
Interleukin 2
Tumor necrosis factors
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(compns. contg. encapsulated **antigens** for immunomodulation)
IT Drug delivery systems
(**controlled-release**; encapsulation of antigens for **controlled release** and immunomodulation)
IT Polyesters, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(dilactone-based; encapsulation of antigens for **controlled release** and immunomodulation)
IT Anaphylaxis
Antigen-presenting cell
Crustacean (Crustacea)
Dendritic cell
Drug targeting
Encapsulation
Endocytosis
Fish
Immunomodulators
Macrophage
Phagocyte
Phagocytosis
(encapsulation of antigens for **controlled release** and immunomodulation)
IT Allergens
Antigens
Biopolymers
Lipids, biological studies
Polymers, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(encapsulation of antigens for **controlled release** and immunomodulation)
IT Autoimmune disease
(encapsulation of antigens for **controlled release** and immunomodulation in autoimmune diseases)
IT **Vaccines**
(encapsulation of antigens for **controlled release** and immunomodulation in relation to **vaccines**)
IT Polymer degradation
(enzymic; encapsulation of antigens for **controlled release** and immunomodulation)
IT T cell (lymphocyte)
(helper cell/inducer, TH1, promotion of; encapsulation of antigens for **controlled release** and immunomodulation)

IT T cell (lymphocyte)
(helper cell/inducer, TH2, suppression of; encapsulation of antigens for **controlled release** and immunomodulation)
IT Drug delivery systems
(injections; encapsulation of antigens for **controlled release** and immunomodulation)
IT Venoms
(insect; encapsulation of antigens for **controlled release** and immunomodulation)
IT Drug delivery systems
(**liposomes**; encapsulation of antigens for **controlled release** and immunomodulation)
IT Cell activation
(lymphocyte; encapsulation of antigens for **controlled release** and immunomodulation)
IT Drug delivery systems
(**microspheres**; encapsulation of antigens for **controlled release** and immunomodulation)
IT Proteins, general, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(milk; encapsulation of antigens for **controlled release** and immunomodulation)
IT Egg, poultry
(proteins; encapsulation of antigens for **controlled release** and immunomodulation)
IT Rubber, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(proteins; encapsulation of antigens for **controlled release** and immunomodulation)
IT Proteins, general, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(soybean; encapsulation of antigens for **controlled release** and immunomodulation)
IT Antibodies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(targeting by; encapsulation of antigens for **controlled release** and immunomodulation)
IT Mucous membrane
(topical delivery to; encapsulation of antigens for **controlled release** and immunomodulation)
IT Drug delivery systems
(topical; encapsulation of antigens for **controlled release** and immunomodulation)
IT Nut (seed)
(tree; encapsulation of antigens for **controlled release** and immunomodulation)
IT Insect (Insecta)
(venoms; encapsulation of antigens for **controlled release** and immunomodulation)
IT **Interferons**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**.gamma.**; compns. contg. encapsulated antigens for immunomodulation)
IT 26780-50-7, Poly(lactide-co-glycolide)
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(encapsulation of antigens for **controlled release** and immunomodulation)

L17 ANSWER 2 OF 6 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:154946 HCAPLUS
DOCUMENT NUMBER: 132:298758
TITLE: **Liposomes** containing **interferon-gamma**. as adjuvant in tumor cell **vaccines**
AUTHOR(S): Van Slooten, M. L.; Storm, G.; Zoephel, A.; Kupcu, Z.; Boerman, O.; Crommelin, D. J. A.; Wagner, E.; Kircheis, R.
CORPORATE SOURCE: Department of Pharmaceutics, Faculty of Pharmacy, Utrecht University, Utrecht, Neth.
SOURCE: Pharm. Res. (2000), 17(1), 42-48
CODEN: PHREEB; ISSN: 0724-8741
PUBLISHER: Kluwer Academic/Plenum Publishers
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Purpose. Liposomal systems may be useful as a cytokine supplement in tumor cell vaccines by providing a cytokine reservoir at the antigen presentation site. Here, we examd. the effect of liposome incorporation of mIFN.gamma. on its potency as adjuvant in an established tumor cell vaccination protocol in the murine B16 melanoma model. Adjuvanticity of the mIFN.gamma.-liposomes was compared to that achieved by mIFN.gamma.-gene transfection of the B16 tumor cells. Furthermore, we studied whether liposomal incorporation of mIFN.gamma. indeed increases the residence time of the cytokine at the vaccination site. Methods. C57B1/6 mice were immunized with irradiated IFN.gamma.-gene transfected B16 melanoma cells or irradiated wild type B16 cells supplemented with (liposomal) mIFN.gamma., followed by a challenge with viable B16 cells. The residence time of the (liposomal) cytokine at the s.c. vaccination site was monitored by using radiolabeled mIFN.gamma. and liposomes. Results. Immunization with irradiated tumor cells admixed with liposomal mIFN.gamma. generated comparable protection against B16 challenge as immunization with mIFN.gamma.-gene modified tumor cells. Irradiated tumor cells admixed with sol. mIFN.gamma. did not generate any protective responses. Radiolabeling studies indicated that free mIFN.gamma. rapidly cleared from the s.c. injection site. Assocn. of [125I]-mIFN.gamma. with liposomes increased the local residence time substantially: liposomal assocn. of mIFN.gamma. resulted in a prolonged local residence time of the cytokine as reflected by a 4-fold increase of the area under the curve. The amt. of released cytokine in the optimal dose range corresponds to the amt. released by the gene-transfected cells. Moderate but significant CTL-activity against B16 cells was found for mice immunized with irradiated cells supplemented with mIFN.gamma.-liposomes compared to untreated control animals. Conclusions. Prolonged presence of mIFN.gamma. at the site of antigen presentation is crucial for the generation of systemic immune responses in the B16 melanoma model. These studies show that liposomal encapsulation of cytokines is an attractive strategy for paracrine cytokine delivery in tumor vaccine development.

CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 3, 15

ST **liposome gamma interferon** adjuvant **vaccine**

IT Immunostimulants
(adjuvants; **liposomes** contg. **.gamma.-interferon** as adjuvants in tumor cell **vaccines**)

IT Lecithins
Phosphatidylglycerols
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(egg yolk; **liposomes** contg. **.gamma.-interferon** as adjuvants in tumor cell **vaccines**)

IT Gene therapy
Transformation, genetic
Vaccines
(**liposomes** contg. **.gamma.-interferon** as adjuvants in tumor cell **vaccines**)

IT Cytokines
RL: BPR (Biological process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(**liposomes** contg. **.gamma.-interferon** as adjuvants in tumor cell **vaccines**)

IT Drug delivery systems
(**liposomes**; **liposomes** contg. **.gamma.-interferon** as adjuvants in tumor cell **vaccines**)

IT **Antitumor agents**
(melanoma; **liposomes** contg. **.gamma.-interferon** as adjuvants in tumor cell **vaccines**)

IT **Interferons**
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**.gamma.**; **liposomes** contg. **.gamma.-interferon** as adjuvants in tumor cell **vaccines**)

REFERENCE COUNT: 30
REFERENCE(S):
(3) Bligh, E; Can J Biochem Physiol 1959, V37, P911 HCAPLUS
(4) Bolton, A; Biochem J 1973, V133, P529 HCAPLUS
(5) Dranoff, G; Proc Natl Acad Sci USA 1993, V90, P3539 HCAPLUS
(6) Hockertz, S; J Interferon Res 1989, V9, P591 HCAPLUS
(7) Hockertz, S; J Interferon Res 1991, V11, P177 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 3 OF 6 HCAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1999:517698 HCAPLUS
DOCUMENT NUMBER: 132:48801
TITLE: Efficient induction of local and systemic antitumor immune response by liposome-mediated intratumoral co-transfer of interleukin-2 gene and interleukin-6 gene
AUTHOR(S): Cao, X.; Wang, Q.; Ju, D. W.; Tao, Q.; Wang, J.
CORPORATE SOURCE: Dept. of Immunology, Second Military Medical University, Shanghai, Peop. Rep. China
SOURCE: J. Exp. Clin. Cancer Res. (1999), 18(2), 191-200
CODEN: JECRDN; ISSN: 0392-9078
PUBLISHER: Regina Elena Institute for Cancer Research
DOCUMENT TYPE: Journal

LANGUAGE: English

AB Interleukin 2 (IL-2) expressing plasmid and interleukin 6 (IL-6)-expressing plasmid were encapsulated in liposome and administered intratumorally into tumor-bearing mice 4 days after s.c. inoculation of B16F10 melanoma cells. The results showed that treatment of tumor-bearing mice with IL-2 gene or IL-6 gene transfer inhibited the growth of s.c. tumor and prolonged the survival of tumor-bearing mice significantly when compared with the treatment of PBS or control gene transfer mediated by liposome. Combined transfer of IL-2 gene and IL-6 gene was found to elicit inhibitory effects on the growth of B16F10 tumor more significantly and prolonged the survival period of tumor-bearing mice more obviously. We investigated the local immunity in tumor microenvironment and found that IL-2 and IL-6 gene transfer could significantly increase the expression of lymphocyte function-assocd. antigen-1 on tumor infiltrating lymphocytes (TIL) and MHC-I mol. on tumor cells freshly isolated from the tumor mass. The NK and CTL activity of TIL increased markedly after the combined transfer of these two cytokine genes. We also obsd. the systemic antitumor immune response in the tumor-bearing mice and demonstrated that NK and CTL activity of splenocytes and the prodn. of IL-2, tumor necrosis factor and interferon-.gamma. from splenocytes increased obviously in mice after the combined transfer of IL-2 and IL-6 gene. In conclusion, local and systemic antitumor immunity of the tumor-bearing host could be induced efficiently after the combined gene transfer. The enhanced specific and non-specific antitumor immunity might be responsible for the more potent antitumor effects of the combined gene therapy.

CC 15-5 (Immunochemistry)

IT **Antitumor agents**
Gene therapy
Plasmid vectors
Vaccines
(efficient induction of local and systemic **antitumor** immune response by liposome-mediated intratumoral co-transfer of interleukin-2 gene and interleukin-6 gene)

IT **Interferons**
RL: MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative)
(.**gamma**.; efficient induction of local and systemic antitumor immune response by **liposome**-mediated intratumoral co-transfer of interleukin-2 gene and interleukin-6 gene)

REFERENCE COUNT: 48

REFERENCE(S):
(1) Bannerji, R; J Immunol 1994, V152, P2324 HCAPLUS
(2) Bui, L; Hum Gene Ther 1997, V8, P2173 HCAPLUS
(3) Caligiuri, M; J Clin Invest 1993, V91, P123 HCAPLUS
(4) Cao, X; Gene Ther 1996, V3, P421 HCAPLUS
(5) Cao, X; J Cancer Res Clin Oncol 1995, V121, P721 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 4 OF 6 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:356622 HCAPLUS

DOCUMENT NUMBER: 131:219067
TITLE: Liposomes as cytokine-supplement in tumor cell-based **vaccines**
AUTHOR(S): van Slooten, Maaike L.; Kircheis, Ralf; Koppenhagen, Frank J.; Wagner, Ernst; Storm, Gert
CORPORATE SOURCE: Department of Pharmaceutics, Utrecht University, Utrecht, 3508 TB, Neth.
SOURCE: Int. J. Pharm. (1999), 183(1), 33-36
CODEN: IJPHDE; ISSN: 0378-5173
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB S.c. vaccination of C57bl/6 mice with irradiated B16 melanoma cells supplemented with liposomal interleukin-2 (IL2) or murine interferon-gamma (mIFN.gamma.), resulted in systemic protection in 50% of the animals against a subsequent tumor cell challenge in a dose-dependent manner. The protective efficacy was comparable to the efficacy of cytokine gene-modified cells as tumor vaccine, whereas irradiated B16 cells supplemented with sol. cytokine did not result in protective responses. In vivo evidence was obtained that the beneficial effects mediated by liposome incorporation of the cytokine are the result of a depot function of the liposomal cytokine supplement at the vaccination site. In can be concluded that liposomal delivery of cytokines offers an attractive alternative to cytokine-gene transfection of tumor cells for therapeutic vaccination protocols.

CC 63-5 (Pharmaceuticals)
Section cross-reference(s): 15
ST melanoma liposome cytokine antitumor **vaccine**
IT Melanoma
(irradiated B16 cells; liposomes as cytokine-supplement in tumor cell-based **vaccines**)
IT Interleukin 2
RL: BAC (Biological activity or effector, except adverse); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(liposomes as cytokine-supplement in tumor cell-based **vaccines**)
IT Drug delivery systems
(liposomes; liposomes as cytokine-supplement in tumor cell-based **vaccines**)
IT **Vaccines**
(tumor; liposomes as cytokine-supplement in tumor cell-based **vaccines**)
IT **Antitumor agents**
(**vaccines**; liposomes as cytokine-supplement in tumor cell-based **vaccines**)
IT **Interferons**
RL: BAC (Biological activity or effector, except adverse); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(.**gamma.**; **liposomes** as cytokine-supplement in tumor cell-based **vaccines**)

REFERENCE COUNT: 17
REFERENCE(S): (1) Abdel Wahab, Z; Cancer Gene Ther 1997, V4, P33 HCAPLUS

(4) Gansbacher, B; J Exp Med 1990, V172, P1217
HCAPLUS
(5) Kircheis, R; Cytokines Cell Mol Ther 1998, V4, P95
HCAPLUS
(6) Koppenhagen, F; Clin Cancer Res 1998, V4, P1881
HCAPLUS
(7) Maass, G; Int J Immunopharmacol 1995, V17, P65
HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 5 OF 6 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:265994 HCAPLUS
DOCUMENT NUMBER: 130:301713
TITLE: Tumor **vaccine**
INVENTOR(S): Wagner, Ernst; Kircheis, Ralf; Crommelin, Daan J. A.; Van Slooten, Maaike
PATENT ASSIGNEE(S): Boehringer Ingelheim International G.m.b.H, Germany
SOURCE: Ger. Offen., 16 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 19746173	A1	19990422	DE 1997-19746173	19971018
WO 9920301	A1	19990429	WO 1998-EP6546	19981015
W: CA, JP, MX, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
EP 1023082	A1	20000802	EP 1998-954420	19981015
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

PRIORITY APPLN. INFO.: DE 1997-19746173 A 19971018
WO 1998-EP6546 W 19981015

AB A tumor vaccine contains, in addn. to a source of tumor antigen, a delayed-release system for interferon-.gamma. (IFN-.gamma.), which releases an effective immunostimulating dose of 50 ng-5 .mu.g IFN-.gamma. during a period of several hours to several days, beginning within 1 h after administration. The delayed-release system for IFN-.gamma. may comprise pegylated liposomes or a biodegradable polymer in the form of microspheres or minipellets. The source of tumor antigen may be (inactivated) autologous or allogenic tumor cells or a tumor cell lysate. Thus, recombinant murine IFN-.gamma. was enclosed in multilamellar phosphatidylcholine-phosphatidylglycerol liposomes; these were mixed with an equal vol. of .gamma.-ray-inactivated, trypsinized mouse 1316F10 melanoma cells and the mixt. was injected s.c. into syngeneic C57Bl/6 mice, followed by a booster injection 1 wk later. The immunization conferred protection from development of implanted B16 melanoma cells in 3-4 of 8 mice.

IC ICM A61K039-00
ICS A61K038-21
CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 15
ST tumor **vaccine interferon gamma**

immunostimulant
IT Melanoma
Tumors (animal)
(cells of, as **antigen** source; **tumor vaccine**
)
IT **Controlled release** drug delivery systems
(**delayed release**; tumor **vaccine**)
IT **Pellets** (drug delivery systems)
(**mini-**; tumor **vaccine**)
IT **Liposomes** (drug delivery systems)
(multilamellar; tumor **vaccine**)
IT Peptides, biological studies
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(of **tumor**-assocd. **antigen**; **tumor vaccine**)
IT **Antigen**-presenting cell
Antitumor agents
Immunostimulants
Liposomes (drug delivery systems)
Melanoma inhibitors
Microspheres (drug delivery systems)
Vaccines
(**tumor vaccine**)
IT **Interferon .gamma.**
Tumor-associated **antigen**
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**tumor vaccine**)

L17 ANSWER 6 OF 6 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1998:113681 HCAPLUS
DOCUMENT NUMBER: 128:203893
TITLE: Immunogenicity and antitumor activity of a liposomal MUC1 peptide-based **vaccine**
AUTHOR(S): Samuel, John; Budzynski, Wladyslaw A.; Reddish, Mark A.; Ding, Lei; Zimmermann, Gabrielle L.; Krantz, Mark J.; Koganty, R. Rao; Longenecker, B. Michael
CORPORATE SOURCE: Fac. of Pharmacy, University of Alberta, Edmonton, AB,
T6N 1H1, Can.
SOURCE: Int. J. Cancer (1998), 75(2), 295-302
CODEN: IJCNAW; ISSN: 0020-7136
PUBLISHER: Wiley-Liss, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A human MUC1-transfected mouse mammary adenocarcinoma cell line (GZHI) was
used to develop both s.c. and i.v. tumor models. A vaccine formulation comprised of a 24 mer (human MUC1) synthetic peptide encapsulated with monophosphoryl lipid A adjuvant (MPLA) in multilamellar liposomes was tested for immunogenicity and antitumor activity. A low dose of the human
MUC1 peptide (5 .mu.g) administered in liposomes provided excellent protection of mice in both tumor challenge models. The protective antitumor activity mediated by the liposome formulation correlated with anti-MUC1-specific T-cell proliferation, gamma-interferon (IFN-.gamma.)

prodn. and IgG2a anti-MUC1 antibodies, suggesting a type I (TI) T-cell response. In contrast, lack of protection in mice immunized with neg. control vaccines correlated with IgG1 anti-MUC1 antibody formation, low or no anti-MUC1 IgG2a and low antigen-specific T-cell proliferation, consistent with a type 2 (T2) T-cell response to the tumor.

CC 15-2 (Immunochemistry)

ST MUC1 peptide **vaccine** immunogenicity tumor

IT **Antitumor agents**
Liposomes (drug delivery systems)
Vaccines
(immunogenicity and **antitumor** activity of a liposomal MUC1 peptide-based **vaccine**)

IT MUC1 mucin
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(immunogenicity and antitumor activity of a liposomal MUC1 peptide-based **vaccine**)

IT T cell (lymphocyte)
(immunogenicity and antitumor activity of a liposomal MUC1 peptide-based **vaccine** in relation to)

IT Antibodies
IgG2a
RL: MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative)
(immunogenicity and antitumor activity of a liposomal MUC1 peptide-based **vaccine** in relation to antibody prodn.)

IT **Interferon .gamma.**
RL: MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative)
(immunogenicity and antitumor activity of a **liposomal** MUC1 peptide-based **vaccine** in relation to **.gamma.-interferon** prodn.)

IT Lipid A
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(monophosphates; immunogenicity and antitumor activity of a liposomal MUC1 peptide-based **vaccine** and a monophosphoryl lipid A adjuvant)

IT 180695-56-1
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(immunogenicity and antitumor activity of a liposomal MUC1 peptide-based **vaccine**)

L18 ANSWER 1 OF 18 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2001:283811 HCAPLUS
DOCUMENT NUMBER: 134:294515
TITLE: Archaeosomes as immunomodulating carriers for acellular **vaccines** to induce cytotoxic T lymphocyte (CTL) responses and protect the **vaccinated** host against intracellular pathogens and cancer
INVENTOR(S): Sprott, G. Dennis; Krishnan, Lakshmi; Conlan, J. Wayne; Omri, Abdel; Patel, Girishchandra B.

PATENT ASSIGNEE(S): National Research Council of Canada, Can.
SOURCE: PCT Int. Appl., 98 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001026683	A2	20010419	WO 2000-CA1197	20001012

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 1999-158944 P 19991012
US 2000-209988 P 20000608

IC ICM A61K039-39
ICS A61K039-00; A61K039-02; A61K009-127; A61P031-04; A61P031-12; A61P035-00
CC 15-2 (Immunochemistry)
Section cross-reference(s): 10
ST archaeosome **vaccine** antigen carrier pathogen cancer
IT Dendritic cell
(CD11c+; archaeosomes as immunomodulating carriers for acellular **vaccines** to induce cytotoxic T lymphocyte responses and protect the **vaccinated** host against intracellular pathogens and cancer)
IT Histocompatibility antigens
RL: BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(MHC (major histocompatibility complex), class I; archaeosomes as immunomodulating carriers for acellular **vaccines** to induce cytotoxic T lymphocyte responses and protect the **vaccinated** host against intracellular pathogens and cancer)
IT Histocompatibility antigens
RL: BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(MHC (major histocompatibility complex), class II; archaeosomes as immunomodulating carriers for acellular **vaccines** to induce cytotoxic T lymphocyte responses and protect the **vaccinated** host against intracellular pathogens and cancer)
IT Animal cell
(Mac 1.alpha.hi; archaeosomes as immunomodulating carriers for acellular **vaccines** to induce cytotoxic T lymphocyte responses and protect the **vaccinated** host against intracellular pathogens and cancer)
IT Proteins, specific or class
RL: PUR (Purification or recovery); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(OMP (outer membrane protein); archaeosomes as immunomodulating carriers for acellular **vaccines** to induce cytotoxic T

lymphocyte responses and protect the **vaccinated** host against intracellular pathogens and cancer)

IT Cell proliferation
(T cell; archaeosomes as immunomodulating carriers for acellular **vaccines** to induce cytotoxic T lymphocyte responses and protect the **vaccinated** host against intracellular pathogens and cancer)

IT Immunostimulants
(adjuvants; archaeosomes as immunomodulating carriers for acellular **vaccines** to induce cytotoxic T lymphocyte responses and protect the **vaccinated** host against intracellular pathogens and cancer)

IT Antigens
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(alkylated; archaeosomes as immunomodulating carriers for acellular **vaccines** to induce cytotoxic T lymphocyte responses and protect the **vaccinated** host against intracellular pathogens and cancer)

IT Animal
Animal virus
Antigen-presenting cell
Archaebacteria (Archaea)
Bacteria (Eubacteria)
CD4-positive T cell
CD8-positive T cell
Francisella tularensis
Halobacterium salinarium
Immunomodulators
Infection
Listeria monocytogenes
Mammal (Mammalia)
Methanobrevibacter smithii
Methanosphaera stadtmanae
Parasite
Pathogen
Protozoa
Thermoplasma acidophilum
Vaccines
(archaeosomes as immunomodulating carriers for acellular **vaccines** to induce cytotoxic T lymphocyte responses and protect the **vaccinated** host against intracellular pathogens and cancer)

IT CD80 (antigen)
CD86 (antigen)
RL: BPR (Biological process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(archaeosomes as immunomodulating carriers for acellular **vaccines** to induce cytotoxic T lymphocyte responses and protect the **vaccinated** host against intracellular pathogens and cancer)

IT CD44 (antigen)
Interleukin 4
Tumor necrosis factors
RL: MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative)
(archaeosomes as immunomodulating carriers for acellular **vaccines** to induce cytotoxic T lymphocyte responses and protect

the **vaccinated** host against intracellular pathogens and cancer)

IT Antibodies
RL: MFM (Metabolic formation); THU (Therapeutic use); BIOL (Biological study); FORM (Formation, nonpreparative); USES (Uses)
(archaeosomes as immunomodulating carriers for acellular **vaccines** to induce cytotoxic T lymphocyte responses and protect the **vaccinated** host against intracellular pathogens and cancer)

IT Glycophospholipids
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(archaetidyl glycerolphosphate-O-Me; archaeosomes as immunomodulating carriers for acellular **vaccines** to induce cytotoxic T lymphocyte responses and protect the **vaccinated** host against intracellular pathogens and cancer)

IT Glycophospholipids
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(archaetidylglycerol; archaeosomes as immunomodulating carriers for acellular **vaccines** to induce cytotoxic T lymphocyte responses and protect the **vaccinated** host against intracellular pathogens and cancer)

IT Drug delivery systems
(carriers; archaeosomes as immunomodulating carriers for acellular **vaccines** to induce cytotoxic T lymphocyte responses and protect the **vaccinated** host against intracellular pathogens and cancer)

IT T cell (lymphocyte)
(cytotoxic; archaeosomes as immunomodulating carriers for acellular **vaccines** to induce cytotoxic T lymphocyte responses and protect the **vaccinated** host against intracellular pathogens and cancer)

IT T cell (lymphocyte)
(helper cell/inducer, TH1, immune response; archaeosomes as immunomodulating carriers for acellular **vaccines** to induce cytotoxic T lymphocyte responses and protect the **vaccinated** host against intracellular pathogens and cancer)

IT T cell (lymphocyte)
(helper cell/inducer, TH2, immune response; archaeosomes as immunomodulating carriers for acellular **vaccines** to induce cytotoxic T lymphocyte responses and protect the **vaccinated** host against intracellular pathogens and cancer)

IT Drug delivery systems
(injections, s.c.; archaeosomes as immunomodulating carriers for acellular **vaccines** to induce cytotoxic T lymphocyte responses and protect the **vaccinated** host against intracellular pathogens and cancer)

IT Drug delivery systems
(**liposomes**, archaeosome; archaeosomes as immunomodulating carriers for acellular **vaccines** to induce cytotoxic T lymphocyte responses and protect the **vaccinated** host against intracellular pathogens and cancer)

IT T cell (lymphocyte)
(marker; archaeosomes as immunomodulating carriers for acellular **vaccines** to induce cytotoxic T lymphocyte responses and protect the **vaccinated** host against intracellular pathogens and

cancer)
IT T cell (lymphocyte)
(memory; archaeosomes as immunomodulating carriers for acellular **vaccines** to induce cytotoxic T lymphocyte responses and protect the **vaccinated** host against intracellular pathogens and cancer)
IT Drug delivery systems
(parenterals; archaeosomes as immunomodulating carriers for acellular **vaccines** to induce cytotoxic T lymphocyte responses and protect the **vaccinated** host against intracellular pathogens and cancer)
IT Lipids, biological studies
RL: PUR (Purification or recovery); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(polar; archaeosomes as immunomodulating carriers for acellular **vaccines** to induce cytotoxic T lymphocyte responses and protect the **vaccinated** host against intracellular pathogens and cancer)
IT Cytokines
RL: MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative)
(prodn.; archaeosomes as immunomodulating carriers for acellular **vaccines** to induce cytotoxic T lymphocyte responses and protect the **vaccinated** host against intracellular pathogens and cancer)
IT T cell (lymphocyte)
(proliferation; archaeosomes as immunomodulating carriers for acellular **vaccines** to induce cytotoxic T lymphocyte responses and protect the **vaccinated** host against intracellular pathogens and cancer)
IT Neoplasm
(solid; archaeosomes as immunomodulating carriers for acellular **vaccines** to induce cytotoxic T lymphocyte responses and protect the **vaccinated** host against intracellular pathogens and cancer)
IT **Antigens**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**tumor**-assocd.; archaeosomes as immunomodulating carriers for acellular **vaccines** to induce cytotoxic T lymphocyte responses and protect the **vaccinated** host against intracellular pathogens and cancer)
IT **Vaccines**
(tumor; archaeosomes as immunomodulating carriers for acellular **vaccines** to induce cytotoxic T lymphocyte responses and protect the **vaccinated** host against intracellular pathogens and cancer)
IT **Antitumor agents**
(**vaccines**; archaeosomes as immunomodulating carriers for acellular **vaccines** to induce cytotoxic T lymphocyte responses and protect the **vaccinated** host against intracellular pathogens and cancer)
IT **Interferons**
RL: MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative)
(.**gamma**.; archaeosomes as immunomodulating carriers for acellular **vaccines** to induce cytotoxic T lymphocyte responses

and protect the **vaccinated** host against intracellular pathogens and cancer)

L18 ANSWER 2 OF 18 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2001:161408 HCAPLUS
DOCUMENT NUMBER: 134:206573
TITLE: Modified binding molecules specific for T lymphocytes and their use as in vivo immune modulators in animals
INVENTOR(S): Chang, Tse Wen
PATENT ASSIGNEE(S): Tanox, Inc., USA
SOURCE: U.S., 9 pp., Cont.-in-part of U.S. 5,872,222.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 6
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6197298	B1	20010306	US 1993-35723	19930323
ZA 9202825	A	19921230	ZA 1992-2825	19920416
US 6129916	A	20001010	US 1992-981276	19921125
US 5872222	A	19990216	US 1992-993291	19921218
WO 9412196	A1	19940609	WO 1993-US11434	19931123
W: AU, BB, BG, BR, CA, FI, HU, JP, KP, KR, LK, MG, MN, MW, NO, PL, RO, RU, SD				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9457292	A1	19940622	AU 1994-57292	19931123

PRIORITY APPLN. INFO.:

US 1991-688000	B2	19910419
US 1992-819449	B2	19920110
US 1992-926566	B2	19920806
US 1992-981276	A2	19921125
US 1992-993291	A2	19921218
US 1993-11130	A	19930128
US 1993-35723	A	19930323
US 1993-46364	A	19930408
US 1993-82742	A	19930625
WO 1993-US11434	W	19931123

IC ICM A61K039-40
NCL 424179100
CC 15-3 (Immunochemistry)
IT Animal
Canine distemper virus
Coronavirus
Diphtheria
Epitopes
Feline leukemia virus
Hepatitis
Human adenovirus
Human herpesvirus 1
Human herpesvirus 2
Immunostimulants
Infection
Influenza
Latex
Melanoma

Pneumonia
Rabies virus
T cell (lymphocyte)
Vaccines
Veterinary medicine
(immunoregulatory substance derived from monoclonal antibody specific for T cell surface antigen increasing activation or proliferation of T lymphocytes)

IT **Tumor** necrosis factors
RL: MFM (Metabolic formation); THU (Therapeutic use); BIOL (Biological study); FORM (Formation, nonpreparative); USES (Uses)
(immunoregulatory substance derived from monoclonal antibody specific for T cell surface **antigen** increasing activation or proliferation of T lymphocytes)

IT Drug delivery systems
(**liposomes**; immunoregulatory substance derived from monoclonal antibody specific for T cell surface antigen increasing activation or proliferation of T lymphocytes)

IT **Interferons**
RL: MFM (Metabolic formation); THU (Therapeutic use); BIOL (Biological study); FORM (Formation, nonpreparative); USES (Uses)
(.**gamma**.; immunoregulatory substance derived from monoclonal antibody specific for T cell surface antigen increasing activation or proliferation of T lymphocytes)

REFERENCE COUNT: 21
REFERENCE(S):
(2) Anon; EP 0336379 1989 HCAPLUS
(4) Anon; WO 9006758 1990 HCAPLUS
(5) Anon; WO 9013281 1990 HCAPLUS
(9) Anon; WO 9206193 1992 HCAPLUS
(10) Anon; WO 9207878 1992 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 3 OF 18 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:855643 HCAPLUS
DOCUMENT NUMBER: 134:16531
TITLE: Implantation of tumor cells for the prevention and treatment of cancer
INVENTOR(S): Brauker, James H.; Geller, Robin Lee; Johnston, William D.; Levon, Steven A.; Maryanov, David A.
PATENT ASSIGNEE(S): Baxter International Inc., USA
SOURCE: U.S., 23 pp., Cont.-in-part of U.S. Ser. No. 272,189, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6156305	A	20001205	US 1995-462252	19950605
JP 10502638	T2	19980310	JP 1995-504331	19950629
NO 9700054	A	19970310	NO 1997-54	19970107

PRIORITY APPLN. INFO.: US 1994-272189 B2 19940708
US 1995-462249 A 19950605
WO 1995-US8151 W 19950629

IC ICM A61K048-00

ICS C12N015-63; C12N005-10; C12N015-09
NCL 424093210
CC 15-2 (Immunochemistry)
Section cross-reference(s): 2, 63
IT **Antitumor agents**
(colon carcinoma; tumor cell implants as)
IT **Antitumor agents**
(fibrosarcoma; tumor cell implants as)
IT **Antitumor agents**
(kidney carcinoma; tumor cell implants as)
IT **Antitumor agents**
(leukemia; tumor cell implants as)
IT Drug delivery systems
(**liposomes**; for administration of cytokines with tumor cell implants)
IT **Antitumor agents**
(lung carcinoma; tumor cell implants as)
IT **Antitumor agents**
(lymphoma; tumor cell implants as)
IT **Antitumor agents**
(mammary gland carcinoma; tumor cell implants as)
IT **Antitumor agents**
(melanoma; tumor cell implants as)
IT **Antitumor agents**
(metastasis; tumor cell implants as)
IT **Antitumor agents**
(neuroblastoma; tumor cell implants as)
IT **Antitumor agents**
(ovary carcinoma; tumor cell implants as)
IT **Antigens**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**tumor**-assocd.; protective immune response against implanted **tumor** cells in relation to)
IT **Vaccines**
(tumor; implantation of tumor cells in)
IT **Antitumor agents**
(**vaccines**; implantation of tumor cells in)
IT **Interferons**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(.**gamma**.; in combination with tumor cell implants for cancer therapy)
REFERENCE COUNT: 71
REFERENCE(S): (6) Anon; EP 0188309 1986 HCAPLUS
(7) Anon; EP 0213908 1987 HCAPLUS
(8) Anon; EP 0232543 1987 HCAPLUS
(24) Cardinal; US 4601893 1986 HCAPLUS
(26) Eckenhoff; US 4684524 1987 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 4 OF 18 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:666966 HCAPLUS
DOCUMENT NUMBER: 133:247277
TITLE: Brefeldin A to enhance peptide presentation by antigen-presenting cells in screening for immunogenic peptides, peptides obtained, and their therapeutic use
INVENTOR(S): Drouet, Emmanuel; Verniol, Cecile; Drouet, Christian

PATENT ASSIGNEE(S): Universite Joseph Fourier - Grenoble 1, Fr.
SOURCE: PCT Int. Appl., 45 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000055622	A1	20000921	WO 2000-FR636	20000316
W: AU, CA, JP, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
FR 2791142	A1	20000922	FR 1999-3304	19990317
FR 2791142	B1	20010622		

PRIORITY APPLN. INFO.: FR 1999-3304 A 19990317
OTHER SOURCE(S): MARPAT 133:247277
IC ICM G01N033-50
ICS C07K014-05; A61K038-00; A61K039-245; A61K009-00; A61K031-365
CC 1-7 (Pharmacology)
Section cross-reference(s): 15, 63
IT **Antitumor agents**
(Burkitt's lymphoma; brefeldin A to enhance peptide presentation by antigen-presenting cells in screening for immunogenic peptides, peptides obtained, and therapeutic use)
IT **Antitumor agents**
(Hodgkin's disease inhibitors; brefeldin A to enhance peptide presentation by antigen-presenting cells in screening for immunogenic peptides, peptides obtained, and therapeutic use)
IT AIDS (disease)
Antigen-presenting cell
Antitumor agents
CD4-positive T cell
CD8-positive T cell
Cytolysis
Dendritic cell
Drug delivery systems
Drug screening
Human herpesvirus 4
Immunostimulants
Immunosuppressants
Immunosuppression
Lymphoblast
Neoplasm
Pathogen
Radiotherapy
Transplant and Transplantation
Virus
(brefeldin A to enhance peptide presentation by antigen-presenting cells in screening for immunogenic peptides, peptides obtained, and therapeutic use)
IT Cytokines
Interleukin 10
Interleukin 12
Interleukin 15
Interleukin 2

Interleukin 6
Lymphokines
Tumor necrosis factors
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(brefeldin A to enhance peptide presentation by **antigen** -presenting cells in screening for immunogenic peptides, peptides obtained, and therapeutic use)

IT Drug delivery systems
(**liposomes**; brefeldin A to enhance peptide presentation by antigen-presenting cells in screening for immunogenic peptides, peptides obtained, and therapeutic use)

IT **Antitumor agents**
(nasopharynx carcinoma; brefeldin A to enhance peptide presentation by antigen-presenting cells in screening for immunogenic peptides, peptides obtained, and therapeutic use)

IT **Interferons**
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(.**gamma**.; brefeldin A to enhance peptide presentation by antigen-presenting cells in screening for immunogenic peptides, peptides obtained, and therapeutic use)

REFERENCE COUNT: 7
REFERENCE(S):
(1) Brigham & Women'S Hospital; WO 9620723 A 1996 HCAPLUS
(2) Grabstein, K; US 5474769 A 1995 HCAPLUS
(3) Hudson, T; US 5112607 A 1992 HCAPLUS
(4) Institut Pasteur de Lyon; WO 9621155 A 1996 HCAPLUS
(5) Johnson & Johnson; WO 9406470 A 1994 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 5 OF 18 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:445172 HCAPLUS
DOCUMENT NUMBER: 134:84788
TITLE: Effective priming of cytotoxic T lymphocyte precursors by subcutaneous administration of peptide antigens in **liposomes** accompanied by anti-CD40 and anti-CTLA-4 antibodies
AUTHOR(S): Ito, Daisuke; Ogasawara, Kazumasa; Matsushita, Kazuhiro; Morohashi, Taiki; Namba, Kenichi; Matsuki, Naoto; Kitaichi, Nobuyoshi; Inuyama, Yukio; Hosokawa, Masuo; Nakayama, Eiichi; Iwabuchi, Kazuya; Onoe, Kazunori
CORPORATE SOURCE: Section of Pathology, Institute of Immunological Science Hokkaido University, Sapporo, Japan
SOURCE: Immunobiology (2000), Volume Date 1999-2000, 201(5), 527-540
CODEN: IMMND4; ISSN: 0171-2985
PUBLISHER: Urban & Fischer Verlag
DOCUMENT TYPE: Journal
LANGUAGE: English
CC 15-2 (Immunochemistry)
Section cross-reference(s): 63
ST **vaccine liposome** peptide CD40 CTLA4 antibody CTL
IT T cell (lymphocyte)
(cytotoxic; effective priming of cytotoxic T lymphocyte precursors by s.c. administration of peptide antigens in **liposomes**

accompanied by anti-CD40 and anti-CTLA-4 antibodies)
IT Dendritic cell
Immunotherapy
Lymph node
Vaccines
(effective priming of cytotoxic T lymphocyte precursors by s.c. administration of peptide antigens in **liposomes** accompanied by anti-CD40 and anti-CTLA-4 antibodies)
IT Peptides, biological studies
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(effective priming of cytotoxic T lymphocyte precursors by s.c. administration of peptide antigens in **liposomes** accompanied by anti-CD40 and anti-CTLA-4 antibodies)
IT Interleukin 12
RL: BOC (Biological occurrence); BIOL (Biological study); OCCU (Occurrence)
(effective priming of cytotoxic T lymphocyte precursors by s.c. administration of peptide antigens in **liposomes** accompanied by anti-CD40 and anti-CTLA-4 antibodies)
IT CD40 (antigen)
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(effective priming of cytotoxic T lymphocyte precursors by s.c. administration of peptide antigens in **liposomes** accompanied by anti-CD40 and anti-CTLA-4 antibodies)
IT CTLA-4 (antigen)
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(effective priming of cytotoxic T lymphocyte precursors by s.c. administration of peptide antigens in **liposomes** accompanied by anti-CD40 and anti-CTLA-4 antibodies)
IT Phosphatidylcholines, biological studies
Phosphatidylserines
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**liposomes** contg.; effective priming of cytotoxic T lymphocyte precursors by s.c. administration of peptide antigens in **liposomes** accompanied by anti-CD40 and anti-CTLA-4 antibodies)
IT Drug delivery systems
(**liposomes**; effective priming of cytotoxic T lymphocyte precursors by s.c. administration of peptide antigens in **liposomes** accompanied by anti-CD40 and anti-CTLA-4 antibodies)
IT Antibodies
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(monoclonal; effective priming of cytotoxic T lymphocyte precursors by s.c. administration of peptide antigens in **liposomes** accompanied by anti-CD40 and anti-CTLA-4 antibodies)
IT **Antigens**
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**tumor**-assocd.; effective priming of cytotoxic T lymphocyte precursors by s.c. administration of peptide **antigens** in **liposomes** accompanied by anti-CD40 and anti-CTLA-4 antibodies)
IT **Interferons**
RL: BOC (Biological occurrence); BIOL (Biological study); OCCU (Occurrence)
(.**gamma**.; effective priming of cytotoxic T lymphocyte precursors by s.c. administration of peptide antigens in

liposomes accompanied by anti-CD40 and anti-CTLA-4 antibodies)
REFERENCE COUNT: 42
REFERENCE(S): (1) Albert, M; Nature 1998, V392, P86 HCAPLUS
(2) Austyn, J; J Exp Med 1996, V183, P1287 HCAPLUS
(3) Banchereau, J; Nature 1998, V392, P245 HCAPLUS
(4) Bennett, S; Nature 1998, V393, P478 HCAPLUS
(5) Carbone, F; J Exp Med 1989, V169, P603 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 6 OF 18 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:240985 HCAPLUS
DOCUMENT NUMBER: 132:292701
TITLE: Novel methods for therapeutic **vaccination**
INVENTOR(S): Steinaa, Lucilla; Mouritsen, Soren; Nielsen, Klaus Gregorious; Haaning, Jesper; Leach, Dana; Dalum, Iben;
Gautam, Anand; Birk, Peter; Karlsson, Gunilla
PATENT ASSIGNEE(S): M Amp E Biotech A/s, Den.
SOURCE: PCT Int. Appl., 220 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000020027	A2	20000413	WO 1999-DK525	19991005
WO 2000020027	A3	20001012		
W: AE, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9958510	A1	20000426	AU 1999-58510	19991005
EP 1117421	A2	20010725	EP 1999-945967	19991005
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, MC, IE, SI, LT, LV, FI, RO				

PRIORITY APPLN. INFO.:

DK 1998-1261	A	19981005
US 1998-105011	P	19981020
WO 1999-DK525	W	19991005

IC A61K039-00
CC 15-2 (Immunochemistry)
Section cross-reference(s): 3, 63
ST weak **antigen vaccine** cytotoxic T lymphocyte; **tumor antigen** T cell epitope **vaccine**
IT Antigens
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(17-1A; weak antigens inserted with foreign T cell epitope as **vaccines**)
IT Antigens
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(AM-1; weak antigens inserted with foreign T cell epitope as **vaccines**)

IT Antigens
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(APC; weak antigens inserted with foreign T cell epitope as **vaccines**)

IT Antigens
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(APRIL; weak antigens inserted with foreign T cell epitope as **vaccines**)

IT Antigens
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(BAGE; weak antigens inserted with foreign T cell epitope as **vaccines**)

IT Chemokines
(C-X-C, Ena78; weak antigens inserted with foreign T cell epitope as **vaccines**)

IT CD antigens
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(CD33; weak antigens inserted with foreign T cell epitope as **vaccines**)

IT Glycoproteins, specific or class
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(CD40-L (antigen CD40 ligand); weak antigens inserted with foreign T cell epitope as **vaccines**)

IT Antigens
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(CD52; weak antigens inserted with foreign T cell epitope as **vaccines**)

IT Antigens
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(CDC27; weak antigens inserted with foreign T cell epitope as **vaccines**)

IT Antigens
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(CO17-1A; weak antigens inserted with foreign T cell epitope as **vaccines**)

IT Antigens
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(CS (circumsporozoite), epitope; weak antigens inserted with foreign T cell epitope as **vaccines**)

IT Proteins, specific or class
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(DCC (deleted in colorectal cancer); weak antigens inserted with foreign T cell epitope as **vaccines**)

IT Antigens
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(DcR3; weak antigens inserted with foreign T cell epitope as **vaccines**)

IT Proteins, specific or class
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(E6; weak antigens inserted with foreign T cell epitope as **vaccines**)
IT Transcription factors
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(E7; weak antigens inserted with foreign T cell epitope as **vaccines**)
IT Hematopoietin receptors
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(FLT3 receptors; weak antigens inserted with foreign T cell epitope as **vaccines**)
IT Glycoproteins, specific or class
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(GP1; weak antigens inserted with foreign T cell epitope as **vaccines**)
IT Proteins, specific or class
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(H-ras; weak antigens inserted with foreign T cell epitope as **vaccines**)
IT Antigens
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(HMTV; weak antigens inserted with foreign T cell epitope as **vaccines**)
IT Heat-shock proteins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(HSP 70; weak antigens inserted with foreign T cell epitope as **vaccines**)
IT Heat-shock proteins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(HSP 90; weak antigens inserted with foreign T cell epitope as **vaccines**)
IT Immunoglobulin receptors
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(IgE type II; weak antigens inserted with foreign T cell epitope as **vaccines**)
IT Proteins, specific or class
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(K-ras; weak antigens inserted with foreign T cell epitope as **vaccines**)
IT Lipoprotein receptors
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(LDL, fusion with FUT or fucosyltransferase; weak antigens inserted with foreign T cell epitope as **vaccines**)
IT Glycoproteins, specific or class
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(MCP (membrane cofactor protein); weak antigens inserted with foreign T
cell epitope as **vaccines**)
IT Multidrug resistance proteins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(MDR1; weak antigens inserted with foreign T cell epitope as **vaccines**)

IT Histocompatibility antigens
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(MHC (major histocompatibility complex), class I; weak antigens inserted with foreign T cell epitope as **vaccines**)

IT Histocompatibility antigens
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(MHC (major histocompatibility complex), class II; weak antigens inserted with foreign T cell epitope as **vaccines**)

IT Diglycerides
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(N-acyl; weak antigens inserted with foreign T cell epitope as **vaccines**)

IT Proteins, specific or class
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(N-ras; weak antigens inserted with foreign T cell epitope as **vaccines**)

IT Glycoproteins, specific or class
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(P170; weak antigens inserted with foreign T cell epitope as **vaccines**)

IT Phosphoproteins
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(P210bcr-c-abl; weak antigens inserted with foreign T cell epitope as **vaccines**)

IT Prostate-specific antigen
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(PSA and PSM; weak antigens inserted with foreign T cell epitope as **vaccines**)

IT Hemopoietins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Progenipoietin; weak antigens inserted with foreign T cell epitope as **vaccines**)

IT Transcription factors
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Rb; weak antigens inserted with foreign T cell epitope as **vaccines**)

IT Antigens
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(SART-1; weak antigens inserted with foreign T cell epitope as **vaccines**)

IT Gene, animal
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(SSX; weak antigens inserted with foreign T cell epitope as **vaccines**)

IT Transcription factors
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(STAT3; weak antigens inserted with foreign T cell epitope as **vaccines**)

IT Mucins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(STn antigen; weak antigens inserted with foreign T cell epitope as **vaccines**)

IT **Antigens**

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(TAG-72 (**tumor**-assocd. glycoprotein 72); weak **antigens** inserted with foreign T cell epitope as **vaccines**)

IT Antigens
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(TPA (tissue protein antigen); weak antigens inserted with foreign T cell epitope as **vaccines**)

IT Proteins, specific or class
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(TRP-1 (tyrosinase-related protein 1); weak antigens inserted with foreign T cell epitope as **vaccines**)

IT Proteins, specific or class
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(TRP-2 (tyrosinase-related protein 2); weak antigens inserted with foreign T cell epitope as **vaccines**)

IT Polyoxyalkylenes, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(adjuvant; weak antigens inserted with foreign T cell epitope as **vaccines**)

IT Immunostimulants
(adjuvants, Freund's incomplete; weak antigens inserted with foreign T cell epitope as **vaccines**)

IT Immunostimulants
(adjuvants, Freund's; weak antigens inserted with foreign T cell epitope as **vaccines**)

IT Immunostimulants
(adjuvants, ISCOMs; weak antigens inserted with foreign T cell epitope as **vaccines**)

IT Immunostimulants
(adjuvants, Ribi; weak antigens inserted with foreign T cell epitope as **vaccines**)

IT Immunostimulants
(adjuvants; weak antigens inserted with foreign T cell epitope as **vaccines**)

IT Drug delivery systems
(anal; weak antigens inserted with foreign T cell epitope as **vaccines**)

IT Animal virus
Bacteria (Eubacteria)
Parasite
(antigen; weak antigens inserted with foreign T cell epitope as **vaccines**)

IT Proteins, specific or class
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(bcl-2; weak antigens inserted with foreign T cell epitope as **vaccines**)

IT Drug delivery systems
(buccal; weak antigens inserted with foreign T cell epitope as **vaccines**)

IT Transcription factors
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(c-myc; weak antigens inserted with foreign T cell epitope as **vaccines**)

IT Diagnosis
(cancer; weak antigens inserted with foreign T cell epitope as **vaccines**)
IT T cell (lymphocyte)
(cytotoxic, epitope; weak antigens inserted with foreign T cell epitope as **vaccines**)
IT Mutation
(deletion; weak antigens inserted with foreign T cell epitope as **vaccines**)
IT Neoplasm
(diagnosis; weak antigens inserted with foreign T cell epitope as **vaccines**)
IT Toxoids
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(diphtheria, epitope; weak antigens inserted with foreign T cell epitope as **vaccines**)
IT Glycophosphoproteins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(endoplasmins; weak antigens inserted with foreign T cell epitope as **vaccines**)
IT Toxins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(enterotoxins, heat-labile; weak antigens inserted with foreign T cell epitope as **vaccines**)
IT Drug delivery systems
(epidural; weak antigens inserted with foreign T cell epitope as **vaccines**)
IT Mucins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(episialins; weak antigens inserted with foreign T cell epitope as **vaccines**)
IT B cell (lymphocyte)
T cell (lymphocyte)
(epitope; weak antigens inserted with foreign T cell epitope as **vaccines**)
IT Hemagglutinins
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(epitope; weak antigens inserted with foreign T cell epitope as **vaccines**)
IT Functional groups
(farnesyl; weak antigens inserted with foreign T cell epitope as **vaccines**)
IT Receptors
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(folate; weak antigens inserted with foreign T cell epitope as **vaccines**)
IT Immunoglobulins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(fragments; weak antigens inserted with foreign T cell epitope as **vaccines**)
IT Vascular endothelial growth factor receptors
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(gene KDR; weak antigens inserted with foreign T cell epitope as **vaccines**)

IT Functional groups
(geranyl-geranyl; weak antigens inserted with foreign T cell epitope as
vaccines)
IT Protein motifs
(glycosylation site; weak antigens inserted with foreign T cell epitope
as **vaccines**)
IT Glycoproteins, specific or class
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(gp100; weak antigens inserted with foreign T cell epitope as
vaccines)
IT Glycoproteins, specific or class
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(gp15; weak antigens inserted with foreign T cell epitope as
vaccines)
IT Sialoglycoproteins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(gp75; weak antigens inserted with foreign T cell epitope as
vaccines)
IT T cell (lymphocyte)
(helper cell, epitope; weak antigens inserted with foreign T cell
epitope as **vaccines**)
IT Phosphoproteins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(hsc 70 (heat-shock cognate, 70,000-mol.-wt.); weak antigens inserted
with foreign T cell epitope as **vaccines**)
IT Drug delivery systems
(injections, s.c.; weak antigens inserted with foreign T cell epitope
as **vaccines**)
IT Mutation
(insertion; weak antigens inserted with foreign T cell epitope as
vaccines)
IT Interleukin receptors
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(interleukin 13 receptors; weak antigens inserted with foreign T cell
epitope as **vaccines**)
IT Drug delivery systems
(intracranial; weak antigens inserted with foreign T cell epitope as
vaccines)
IT Drug delivery systems
(intracutaneous; weak antigens inserted with foreign T cell epitope as
vaccines)
IT Drug delivery systems
(intradermal; weak antigens inserted with foreign T cell epitope as
vaccines)
IT Hemolysins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(listeriolysins; weak antigens inserted with foreign T cell epitope as
vaccines)
IT Proteins, specific or class
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(mammaglobin; weak antigens inserted with foreign T cell epitope as
vaccines)
IT Antigens
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(melanoma-assocd., MAGE; weak antigens inserted with foreign T cell

epitope as **vaccines**)
IT Antigens
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(melanoma-assocd., Melan-A/MART-1; weak antigens inserted with foreign T cell epitope as **vaccines**)
IT Transferrins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(melanotransferrins; weak antigens inserted with foreign T cell epitope as **vaccines**)
IT Chromosome
(minichromosomes; weak antigens inserted with foreign T cell epitope as **vaccines**)
IT Chemicals
(modification; weak antigens inserted with foreign T cell epitope as **vaccines**)
IT Mucins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(mucin 2, 3 and 4; weak antigens inserted with foreign T cell epitope as **vaccines**)
IT Functional groups
(myristyl; weak antigens inserted with foreign T cell epitope as **vaccines**)
IT DNA
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(naked; weak antigens inserted with foreign T cell epitope as **vaccines**)
IT Mammary gland
Prostate gland
(neoplasm; weak antigens inserted with foreign T cell epitope as **vaccines**)
IT Microorganism
(non-pathogenic; weak antigens inserted with foreign T cell epitope as **vaccines**)
IT Liquids
(oils formulation; weak antigens inserted with foreign T cell epitope as **vaccines**)
IT Drug delivery systems
(oral; weak antigens inserted with foreign T cell epitope as **vaccines**)
IT Proteins, specific or class
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(p15; weak antigens inserted with foreign T cell epitope as **vaccines**)
IT Functional groups
(palmitoyl; weak antigens inserted with foreign T cell epitope as **vaccines**)
IT Drug delivery systems
(parenterals; weak antigens inserted with foreign T cell epitope as **vaccines**)
IT Drug delivery systems
(peritoneal; weak antigens inserted with foreign T cell epitope as **vaccines**)
IT Glycolipoproteins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(phosphatidylinositol-contg.; weak antigens inserted with foreign T cell epitope as **vaccines**)
IT Proteins, specific or class
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(probasins; weak antigens inserted with foreign T cell epitope as **vaccines**)
IT Glycoproteins, specific or class
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(prostateins; weak antigens inserted with foreign T cell epitope as **vaccines**)
IT Interleukin 13
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(receptors; weak antigens inserted with foreign T cell epitope as **vaccines**)
IT Proteins, specific or class
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(self; weak antigens inserted with foreign T cell epitope as **vaccines**)
IT Drug delivery systems
(spinal; weak antigens inserted with foreign T cell epitope as **vaccines**)
IT Drug delivery systems
(subdermal; weak antigens inserted with foreign T cell epitope as **vaccines**)
IT Drug delivery systems
(sublingual; weak antigens inserted with foreign T cell epitope as **vaccines**)
IT Mutation
(substitution; weak antigens inserted with foreign T cell epitope as **vaccines**)
IT Antigens
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(surface; weak antigens inserted with foreign T cell epitope as **vaccines**)
IT Genetic element
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(terminator; weak antigens inserted with foreign T cell epitope as **vaccines**)
IT Toxoids
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(tetanus, epitope; weak antigens inserted with foreign T cell epitope as **vaccines**)
IT Proteins, specific or class
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(transfection-facilitating; weak antigens inserted with foreign T cell epitope as **vaccines**)
IT Proteins, specific or class
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(transmembrane, mesothelin; weak antigens inserted with foreign T cell epitope as **vaccines**)
IT **Antigens**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**tumor**-assocd., G250; weak **antigens** inserted with foreign T cell epitope as **vaccines**)

IT **Antigens**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**tumor**-assocd., GAGE; weak **antigens** inserted with foreign T cell epitope as **vaccines**)

IT **Antigens**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**tumor**-assocd., KIAA0205 bladder carcinoma **antigen**; weak **antigens** inserted with foreign T cell epitope as **vaccines**)

IT **Antigens**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**tumor**-assocd., MAP17; weak **antigens** inserted with foreign T cell epitope as **vaccines**)

IT **Antigens**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**tumor**-assocd., MIC A/B; weak **antigens** inserted with foreign T cell epitope as **vaccines**)

IT **Antigens**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**tumor**-assocd., MUM-1; weak **antigens** inserted with foreign T cell epitope as **vaccines**)

IT **Antigens**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**tumor**-assocd., NY-ESO-1; weak **antigens** inserted with foreign T cell epitope as **vaccines**)

IT **Antigens**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**tumor**-assocd., PRAME; weak **antigens** inserted with foreign T cell epitope as **vaccines**)

IT **Antigens**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**tumor**-assocd., Pmel-17; weak **antigens** inserted with foreign T cell epitope as **vaccines**)

IT **Antigens**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**tumor**-assocd., RCAS1; weak **antigens** inserted with foreign T cell epitope as **vaccines**)

IT **Antigens**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**tumor**-assocd., ZAG; weak **antigens** inserted with foreign T cell epitope as **vaccines**)

IT **Antigens**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**tumor**-assocd., p16INK4; weak **antigens** inserted with foreign T cell epitope as **vaccines**)

IT **Antigens**
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**tumor**-assocd.; weak **antigens** inserted with foreign T cell epitope as **vaccines**)

IT **Antigens**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**tumor**-rejection, RAGE-1; weak **antigens** inserted with foreign T cell epitope as **vaccines**)

IT Complement receptors
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(type 1; weak antigens inserted with foreign T cell epitope as **vaccines**)

IT Complement receptors
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(type 2; weak antigens inserted with foreign T cell epitope as **vaccines**)

IT Animal
Animal cell line
Antigen-presenting cell
Antitumor agents
Bacteriophage
Carriers
Cosmids
DNA sequences
Dendritic cell
Encapsulation
Epitopes
Immunotherapy
Influenza virus
Latex
Liposomes
Macrophage
Micelles
Molecular cloning
Mycobacterium
Particles
Plasmids
Plasmodium falciparum
Protein sequences
Quillaja saponaria
Vaccines
Virus
Virus vectors
(weak antigens inserted with foreign T cell epitope as **vaccines**)

IT Gene, animal
Promoter (genetic element)
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(weak antigens inserted with foreign T cell epitope as **vaccines**)

IT CA 125 (carbohydrate antigen)
CD19 (antigen)
CD20 (antigen)
CD22 (antigen)
CD44 (antigen)
CD45 (antigen)
CD5 (antigen)
CD59 (antigen)
Carcinoembryonic antigen
Enzymes, biological studies
Epidermal growth factor receptors
Haptens
.alpha.-Fetoproteins
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(weak antigens inserted with foreign T cell epitope as **vaccines**

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IT Antibodies
Antigens
CD40 (antigen)
CTLA-4 (antigen)
Calreticulin
Carbohydrates, biological studies
Cytokines
DNA
Heat-shock proteins
Insulin-like growth factor I receptors
Interleukin 1
Interleukin 12
Interleukin 13
Interleukin 15
Interleukin 2
Interleukin 4
Interleukin 6
Ki-67 antigen
Lipid A
Lipids, biological studies
Osteonectin
Plastics, biological studies
Platelet-derived growth factors
Polymers, biological studies
Receptors
Saponins
Toxins
Tumor necrosis factors
neu (receptor)
p53 (protein)
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(weak **antigens** inserted with foreign T cell epitope as **vaccines**)
IT Transforming growth factors
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(.alpha.-; weak antigens inserted with foreign T cell epitope as **vaccines**)
IT Catenins
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(.beta.-; weak antigens inserted with foreign T cell epitope as **vaccines**)
IT Transforming growth factors
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(.beta.-; weak antigens inserted with foreign T cell epitope as **vaccines**)
IT **Interferons**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(.**gamma**.; weak antigens inserted with foreign T cell epitope as **vaccines**)
IT 39391-18-9
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(2; weak antigens inserted with foreign T cell epitope as **vaccines**)
IT 62031-54-3, FGF

RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(8a and 8b isoforms; weak antigens inserted with foreign T cell epitope as **vaccines**)

IT 264178-47-4P
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(P2 epitope gene; weak antigens inserted with foreign T cell epitope as **vaccines**)

IT 126779-13-3P
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(P2 epitope; weak antigens inserted with foreign T cell epitope as **vaccines**)

IT 264185-70-8P
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(P30 epitope gene; weak antigens inserted with foreign T cell epitope as **vaccines**)

IT 126779-14-4P
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(P30 epitope; weak antigens inserted with foreign T cell epitope as **vaccines**)

IT 99-20-7D, Trehalose, diester 7429-90-5, Aluminum, biological studies 9004-54-0, Dextran, biological studies 9005-25-8, Starch, biological studies 25322-68-3 53678-77-6, Muramyl dipeptide
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(adjuvant; weak antigens inserted with foreign T cell epitope as **vaccines**)

IT 148997-75-5, Androgen-induced growth factor (mouse clone pSC17 precursor reduced) 264179-58-0 264179-59-1, Neu (receptor) (human) 264179-62-6
264179-64-8 264179-65-9 264179-66-0 264179-67-1 264179-68-2
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(amino acid sequence; weak antigens inserted with foreign T cell epitope as **vaccines**)

IT 3458-28-4, Mannose 9036-88-8, Mannan
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(binding partner; weak antigens inserted with foreign T cell epitope as **vaccines**)

IT 56093-23-3
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(fusion with LDL receptor; weak antigens inserted with foreign T cell epitope as **vaccines**)

IT 125978-95-2, Nitric oxide synthase
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inducible; weak antigens inserted with foreign T cell epitope as

vaccines)
IT 9030-23-3, Thymidine phosphorylase
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inhibitor; weak antigens inserted with foreign T cell epitope as **vaccines**)
IT 141907-41-7, Matrix metalloproteinase
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(isoforms; weak antigens inserted with foreign T cell epitope as **vaccines**)
IT 100040-73-1, DNA (human clone .lambda.HER2-436 gene HER2 receptor cDNA) 264179-57-9 264179-60-4 264179-61-5 264179-63-7
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(nucleotide sequence; weak antigens inserted with foreign T cell epitope as **vaccines**)
IT 52-90-4, Cysteine, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(residue; weak antigens inserted with foreign T cell epitope as **vaccines**)
IT 217865-15-1 259127-00-9, 9: PN: US6027895 SEQID: 10 unclaimed DNA 264179-74-0 264179-76-2 264179-77-3
RL: PRP (Properties)
(unclaimed nucleotide sequence; novel methods for therapeutic **vaccination**)
IT 179920-34-4
RL: PRP (Properties)
(unclaimed protein sequence; novel methods for therapeutic **vaccination**)
IT 64134-30-1 137219-78-4 264134-74-9 264134-75-0 264134-76-1 264134-77-2 264179-75-1
RL: PRP (Properties)
(unclaimed sequence; novel methods for therapeutic **vaccination**)
IT 264134-70-5P 264134-71-6P 264134-72-7P 264134-73-8P 264134-78-3P 264224-61-5P 264224-76-2P
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(weak antigens inserted with foreign T cell epitope as **vaccines**)
IT 71965-46-3, Cathepsins 99085-47-9, Complement decay-accelerating factor 147014-97-9, Cyclin-dependent kinase 4 179241-78-2, Caspase 8
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(weak antigens inserted with foreign T cell epitope as **vaccines**)
IT 251541-10-3, Human Her2 protein (59-73) 251542-12-8, Human Her2 protein (465-479) 264617-99-4, Human PSM (87-108) 264618-03-3, Human PSM (210-230) 264618-06-6, Human PSM (269-289) 264618-07-7, Human PSM (298-324) 264618-08-8, Human PSM (442-465) 264618-09-9, Human PSM (488-514) 264618-23-7, Human PSM (598-630) 264619-18-3, Human PSM (643-662) 264619-84-3, Human PSM (672-699) 264620-57-7, Human Her2 protein (5-25) 264620-84-0, Human Her2 protein (103-117) 264621-04-7, Human Her2 protein (149-163) 264621-94-5, Human Her2 protein (210-224) 264622-06-2, Human Her2 protein (250-264) 264622-08-4, Human Her2 protein (325-339) 264622-09-5, Human Her2 protein (369-383) 264622-23-3, Human Her2 protein (579-593) 264624-69-3, Human Her2

protein (632-652) 264624-79-5, Human Her2 protein (653-667) 264624-80-8, Human Her2 protein (661-675) 264625-23-2, Human Her2 protein (695-709) 264625-25-4, Human Her2 protein (72-86) 264625-36-7, Human Her2 protein (146-160) 264625-37-8, Human Her2 protein (221-235) 264625-38-9, Human Her2 protein (257-271) 264625-51-6, Human FGF8b protein (1-54) 264626-02-0, Human FGF8b protein (55-58) 264626-17-7, Human FGF8b protein (178-215) 264626-69-9, Human FGF8b protein (63-68) 264626-82-6, Human FGF8b protein (72-76) 264626-84-8, Human FGF8b protein (85-91) 264626-85-9, Human FGF8b protein (95-102) 264626-86-0, Human FGF8b protein (106-111) 264626-87-1, Human FGF8b protein (115-120) 264627-05-6, Human FGF8b protein (128-134) 264627-07-8, Human FGF8b protein (138-144) 264627-09-0, Human FGF8b protein (149-154) 264627-10-3, Human FGF8b protein (158-162) 264627-11-4, Human FGF8b protein (173-177) 264627-12-5, Human FGF8b protein (26-45)
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(weak antigens inserted with foreign T cell epitope as **vaccines**)

IT 3700-67-2 9001-91-6, Plasminogen 9002-10-2, Tyrosinase 9002-61-3, Human chorionic gonadotropin 9032-22-8, Mox1 oxidase 9034-40-6, Gonadotropin-releasing hormone 9081-34-9, 5.alpha. Reductase 50812-37-8, Glutathione S-transferase 60748-06-3, Gastrin 17 62010-37-1, GD3 65988-71-8, GD2 66456-69-7, GM4 66594-14-7, Quil A 80043-53-4, Gastrin-releasing peptide 83588-90-3, N-Acetylglucosaminyltransferase V 83869-56-1, GM-CSF 89800-66-8, Heparanase 120178-12-3, Telomerase 127464-60-2, Vascular endothelial growth factor 140208-23-7, Plasminogen activator inhibitor-1 141256-04-4, QS21
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(weak antigens inserted with foreign T cell epitope as **vaccines**)

IT 61512-21-8, Thymosin
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(.beta. 15; weak antigens inserted with foreign T cell epitope as **vaccines**)

IT 9005-80-5, Inulin
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(.gamma.-; weak antigens inserted with foreign T cell epitope as **vaccines**)

L18 ANSWER 7 OF 18 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:819202 HCAPLUS
DOCUMENT NUMBER: 132:69325
TITLE: Systemic immune activation method using nucleic acid-lipid complexes
INVENTOR(S): Dow, Steven W.; Elmslie, Robyn E.; Schwarze, Jurgen Karl Johannes
PATENT ASSIGNEE(S): National Jewish Medical and Research Center, USA
SOURCE: PCT Int. Appl., 115 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9966879	A2	19991229	WO 1999-US14015	19990622
WO 2000066879	A3	20000302		

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 1998-104759 19980625

IC ICM A61K

CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 15

ST immunostimulant **vaccine** nucleic acid complex

IT **Vaccines**
(antigen-nonspecific; systemic immune activation method using nucleic acid-lipid complexes)

IT **Antitumor agents**
(bladder carcinoma; systemic immune activation method using nucleic acid-lipid complexes)

IT **Antitumor agents**
(brain; systemic immune activation method using nucleic acid-lipid complexes)

IT **Antitumor agents**
(digestive tract; systemic immune activation method using nucleic acid-lipid complexes)

IT **Antitumor agents**
(head carcinoma; systemic immune activation method using nucleic acid-lipid complexes)

IT **Antitumor agents**
(hemangiosarcoma; systemic immune activation method using nucleic acid-lipid complexes)

IT **Antitumor agents**
(hepatoma; systemic immune activation method using nucleic acid-lipid complexes)

IT Drug delivery systems
(**liposomes**; systemic immune activation method using nucleic acid-lipid complexes)

IT **Antitumor agents**
(lung; systemic immune activation method using nucleic acid-lipid complexes)

IT **Antitumor agents**
(mammary gland; systemic immune activation method using nucleic acid-lipid complexes)

IT **Antitumor agents**
(melanoma; systemic immune activation method using nucleic acid-lipid complexes)

IT **Antitumor agents**
(metastasis; systemic immune activation method using nucleic acid-lipid
complexes)

IT **Antitumor agents**
(neck carcinoma; systemic immune activation method using nucleic acid-lipid complexes)
IT **Vaccines**
(nucleic acid; systemic immune activation method using nucleic acid-lipid complexes)
IT **Antitumor agents**
(ovary; systemic immune activation method using nucleic acid-lipid complexes)
IT **Antitumor agents**
(pancreas; systemic immune activation method using nucleic acid-lipid complexes)
IT **Antitumor agents**
(prostate gland; systemic immune activation method using nucleic acid-lipid complexes)
IT **Antitumor agents**
(renal cell carcinoma; systemic immune activation method using nucleic acid-lipid complexes)
IT **Antitumor agents**
(skin; systemic immune activation method using nucleic acid-lipid complexes)
IT **Antitumor agents**
(soft tissue sarcoma; systemic immune activation method using nucleic acid-lipid complexes)
IT **Antitumor agents**
(squamous cell carcinoma; systemic immune activation method using nucleic acid-lipid complexes)
IT AIDS (disease)
Anti-inflammatory agents
Antitumor agents
Antiviral agents
Candida
Canidae
Cat (Felis catus)
Cattle
Food allergy
Horse (Equus caballus)
Human herpesvirus
Human immunodeficiency virus
Immunization
Immunostimulants
Mouse
Mycobacterium tuberculosis
Papillomavirus
Pathogenic bacteria
Pollen
Rat
Sheep
Swine
Testis, neoplasm
(systemic immune activation method using nucleic acid-lipid complexes)
IT **Antitumor agents**
(thyroid gland carcinoma; systemic immune activation method using nucleic acid-lipid complexes)
IT mRNA
RL: BAC (Biological activity or effector, except adverse); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological

study); PROC (Process); USES (Uses)
(**tumor antigen**-specifying; systemic immune activation method using nucleic acid-lipid complexes)
IT B cell (lymphocyte)
T cell (lymphocyte)
(**tumor antigens** recognized by; systemic immune activation method using nucleic acid-lipid complexes)
IT **Antigens**
RL: BAC (Biological activity or effector, except adverse); BOC (Biological occurrence); BPR (Biological process); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(**tumor**-assocd.; systemic immune activation method using nucleic acid-lipid complexes)
IT **Vaccines**
(tumor; systemic immune activation method using nucleic acid-lipid complexes)
IT **Antitumor agents**
(**vaccines**; systemic immune activation method using nucleic acid-lipid complexes)
IT **Interferons**
RL: MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative)
(.**gamma**.; systemic immune activation method using nucleic acid-lipid complexes)

L18 ANSWER 8 OF 18 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:468593 HCAPLUS
DOCUMENT NUMBER: 131:101258
TITLE: Materials and methods for treating oncological disease
INVENTOR(S): Lawman, Patricia; Lawman, Michael J. P.
PATENT ASSIGNEE(S): Morphogenesis, Inc., USA
SOURCE: PCT Int. Appl., 37 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9936433	A2	19990722	WO 1999-US787	19990114
WO 9936433	A3	19990923		

W: CA, JP, US
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE
PRIORITY APPLN. INFO.: US 1998-71497 P 19980114
IC ICM C07K014-00
CC 15-2 (Immunochemistry)
Section cross-reference(s): 3
IT Histocompatibility **antigens**
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(MHC (major histocompatibility **antigen** complex), class I; transformed **tumor** cells encoding a superantigen and a

bacterial or eukaryotic protein for treating oncol. disease)

IT Histocompatibility **antigens**
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(MHC (major histocompatibility **antigen** complex), class II, -DR4; transformed **tumor** cells encoding a superantigen and a bacterial or eukaryotic protein for treating oncol. disease)

IT Histocompatibility **antigens**
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(MHC (major histocompatibility **antigen** complex), class II; transformed **tumor** cells encoding a superantigen and a bacterial or eukaryotic protein for treating oncol. disease)

IT Histocompatibility **antigens**
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(MHC (major histocompatibility complex), class III; transformed **tumor** cells encoding a superantigen and a bacterial or eukaryotic protein for treating oncol. disease)

IT Histocompatibility **antigens**
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(MHC (major histocompatibility complex); transformed **tumor** cells encoding a superantigen and a bacterial or eukaryotic protein for
treating oncol. disease)

IT Mycobacterium
(**antigen**; transformed **tumor** cells encoding a superantigen and a bacterial or eukaryotic protein for treating oncol. disease)

IT **Vaccines**
(cancer; transformed tumor cells encoding a superantigen and a bacterial or eukaryotic protein for treating oncol. disease)

IT **Antigens**
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(hyperacute rejection; transformed **tumor** cells encoding a superantigen and a bacterial or eukaryotic protein for treating oncol. disease)

IT **Antigens**
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(superantigens; transformed **tumor** cells encoding a superantigen and a bacterial or eukaryotic protein for treating oncol. disease)

IT Adeno-associated virus
Adenoviridae
Antitumor agents
Bacteria (Eubacteria)
Brain, neoplasm
Carcinoma

Chemotherapy
DNA sequences
Dendritic cell
Domestic animal
Eukaryote (Eukaryotae)
Genetic vectors
Herpesviridae
Leukemia
Liposomes
Lymphoma
Melanoma
Neoplasm
Plasmids
Poxviridae
Radiotherapy
Retroviridae
Sarcoma
Streptococcus group A
Surgery
Swine
Virus
(transformed tumor cells encoding a superantigen and a bacterial or eukaryotic protein for treating oncol. disease)

IT **Antigens**
Cytokines
DNA
Gene, animal
Gene, microbial
Interleukin 1
Interleukin 2
Interleukin 3
Interleukin 4
Macrophage inflammatory protein 1.alpha.
Macrophage inflammatory protein 1.beta.
Polynucleotides
Tumor necrosis factors
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(transformed **tumor** cells encoding a superantigen and a bacterial or eukaryotic protein for treating oncol. disease)

IT **Interferons**
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(.**gamma**.; transformed tumor cells encoding a superantigen and a bacterial or eukaryotic protein for treating oncol. disease)

L18 ANSWER 9 OF 18 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:468570 HCAPLUS
DOCUMENT NUMBER: 131:115306
TITLE: Patient-specific white blood cell malignancy **vaccine** from membrane-proteoliposomes
INVENTOR(S): Popescu, Mircea C.; Boni, Lawrence; Robb, Richard J.; Batenjany, Michael M.
PATENT ASSIGNEE(S): Biomira USA Inc., USA
SOURCE: PCT Int. Appl., 22 pp.

CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9936085	A1	19990722	WO 1999-US935	19990115
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9920318	A1	19990802	AU 1999-20318	19990115
EP 1045698	A1	20001025	EP 1999-900822	19990115
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
US 6207170	B1	20010327	US 1999-231650	19990115
US 2001012517	A1	20010809	US 2001-816266	20010326

PRIORITY APPLN. INFO.:
US 1998-71702 P 19980116
US 1999-231650 A1 19990115
WO 1999-US935 W 19990115

IC ICM A61K039-00
CC 15-2 (Immunochemistry)
Section cross-reference(s): 63
ST patient specific antitumor **vaccine** leukemia **liposome**
IT Cell adhesion molecules
RL: BAC (Biological activity or effector, except adverse); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(ICAM-1 (intercellular adhesion mol. 1); patient-specific white blood cell malignancy **vaccine** from membrane-proteoliposomes)
IT Histocompatibility antigens
RL: BAC (Biological activity or effector, except adverse); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(MHC (major histocompatibility complex), exogenous; patient-specific white blood cell malignancy **vaccine** from membrane-proteoliposomes)
IT Immunostimulants
(adjuvants; patient-specific white blood cell malignancy **vaccine** from membrane-proteoliposomes)
IT Lymphoma
Multiple myeloma
(cell membrane components from; patient-specific white blood cell malignancy **vaccine** from membrane-proteoliposomes)
IT Lipids, biological studies
RL: BAC (Biological activity or effector, except adverse); PEP (Physical, engineering or chemical process); BIOL (Biological study); PROC (Process)
(exogenous; patient-specific white blood cell malignancy **vaccine** from membrane-proteoliposomes)
IT **Antitumor agents**

(leukemia; patient-specific white blood cell malignancy **vaccine** from membrane-proteoliposomes)

IT Cell membrane
(malignancy-derived; patient-specific white blood cell malignancy **vaccine** from membrane-proteoliposomes)

IT Lipid A
RL: BAC (Biological activity or effector, except adverse); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(monophosphates; patient-specific white blood cell malignancy **vaccine** from membrane-proteoliposomes)

IT Immunostimulants
Leukemia
Vaccines
(patient-specific white blood cell malignancy **vaccine** from membrane-proteoliposomes)

IT CD80 (antigen)
CD86 (antigen)
Cytokines
Glycolipids
Interferons
Interleukin 2
Lipid A
Lymphokines
Phospholipids, biological studies
RL: BAC (Biological activity or effector, except adverse); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(patient-specific white blood cell malignancy **vaccine** from membrane-proteoliposomes)

IT **Liposomes**
(proteoliposomes, malignant cell membrane-contg.; patient-specific white blood cell malignancy **vaccine** from membrane-proteoliposomes)

IT **Antigens**
RL: BAC (Biological activity or effector, except adverse); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(**tumor**-specific **antigens**; patient-specific white blood cell malignancy **vaccine** from membrane-proteoliposomes)

IT **Interferons**
RL: BAC (Biological activity or effector, except adverse); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(.**gamma**.; patient-specific white blood cell malignancy **vaccine** from membrane-proteoliposomes)

IT 57-88-5, Cholesterol, biological studies 2644-64-6, 1,2-Dipalmitoylphosphatidylcholine 18194-24-6, 1,2-Dimyristoylphosphatidylcholine 53678-77-6, Muramyl dipeptide 61361-72-6, Dimyristoylphosphatidylglycerol 81627-83-0, Mcsf 83869-56-1, Gmcsf
RL: BAC (Biological activity or effector, except adverse); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(patient-specific white blood cell malignancy **vaccine** from membrane-proteoliposomes)

REFERENCE COUNT: 4

REFERENCE(S):
(1) Farmacoterapico Ist Ital; EP 0283443 A 1988 HCAPLUS
(2) Jean-Claude, B; US 5635188 A 1997 HCAPLUS
(3) Larry, K; WO 9729769 A 1997 HCAPLUS
(4) Zintl, F; ZEITSCHRIFT FUR DIE GESAMTE INNERE MEDIZIN UND IHRE GRENZGEBIETE 1976, V31(8), P227 MEDLINE

L18 ANSWER 10 OF 18 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:388085 HCAPLUS
DOCUMENT NUMBER: 131:43575
TITLE: Methods for enhancement of protective immune responses employing leishmania polypeptides
INVENTOR(S): Reed, Steven G.
PATENT ASSIGNEE(S): Corixa Corporation, USA
SOURCE: PCT Int. Appl., 108 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 7
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9929341	A2	19990617	WO 1998-US26438	19981211
WO 9929341	A3	19991028		
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6013268	A	20000111	US 1997-989370	19971212
AU 9917249	A1	19990628	AU 1999-17249	19981211

PRIORITY APPLN. INFO.:

US 1997-989370	A	19971212
US 1994-232534	B2	19940422
US 1995-454036	A2	19950530
US 1995-488386	B2	19950606
US 1996-607509	A2	19960223
US 1996-634642	A2	19960418
WO 1998-US26438	W	19981211

IC ICM A61K039-008
ICS C07K014-44; C12N015-30; A61K039-008; A61K045-05
CC 15-2 (Immunochemistry)
Section cross-reference(s): 3
ST Leishmania braziliensis eukaryotic initiation factor 4A; eukaryotic initiation factor 4A Leishmania major; LbeIF4A LmeIF4A Leishmania **vaccine tumor antigen**
IT Immunoglobulins
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Fc region; **vaccine** comprising or DNA **vaccine** encoding **antigen** or **tumor antigen** and LbeIF-4A and LmeIF-4A)

IT Gene, microbial
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(LbeIF4A and LmeIF4A; **vaccine** comprising or DNA **vaccine** encoding **antigen** or **tumor antigen** and LbeIF-4A and LmeIF-4A)

IT Initiation factors (protein formation)
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(LbeIF4A; **vaccine** comprising or DNA **vaccine** encoding **antigen** or **tumor antigen** and LbeIF-4A and LmeIF-4A)

IT Initiation factors (protein formation)
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(LmeIF4A; **vaccine** comprising or DNA **vaccine** encoding **antigen** or **tumor antigen** and LbeIF-4A and LmeIF-4A)

IT Immunity
(Th1 and Th2; **vaccine** comprising or DNA **vaccine** encoding **antigen** or **tumor antigen** and LbeIF-4A and LmeIF-4A)

IT Cytokines
RL: BSU (Biological study, unclassified); MFM (Metabolic formation); THU (Therapeutic use); BIOL (Biological study); FORM (Formation, nonpreparative); USES (Uses)
(Th1 and Th2; **vaccine** comprising or DNA **vaccine** encoding **antigen** or **tumor antigen** and LbeIF-4A and LmeIF-4A)

IT Disease, animal
(Th1- or Th2-assocd.; **vaccine** comprising or DNA **vaccine** encoding **antigen** or **tumor antigen** and LbeIF-4A and LmeIF-4A)

IT Autoimmune disease
(Th2-assocd.; **vaccine** comprising or DNA **vaccine** encoding **antigen** or **tumor antigen** and LbeIF-4A and LmeIF-4A)

IT **Microspheres**
(biodegradable; **vaccine** comprising or DNA **vaccine** encoding **antigen** or **tumor antigen** and LbeIF-4A and LmeIF-4A)

IT Immunity
(cell-mediated; **vaccine** comprising or DNA **vaccine** encoding **antigen** or **tumor antigen** and LbeIF-4A and LmeIF-4A)

IT T cell (lymphocyte)
(cytotoxic; **vaccine** comprising or DNA **vaccine** encoding **antigen** or **tumor antigen** and LbeIF-4A and LmeIF-4A)

IT Initiation factors (protein formation)
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(eIF-4A, homologs derived from Leishmania braziliensis or Leishmania major; **vaccine** comprising or DNA **vaccine** encoding

antigen or **tumor antigen** and LbeIF-4A and LmeIF-4A)

IT Interleukin 12
Interleukin 15
Interleukin 18
Interleukin 2
RL: BOC (Biological occurrence); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); USES (Uses)
(enhancement of Th1-assocd. cytokines; **vaccine** comprising or DNA **vaccine** encoding **antigen** or **tumor antigen** and LbeIF-4A and LmeIF-4A)

IT Immunity
(humoral; **vaccine** comprising or DNA **vaccine** encoding **antigen** or **tumor antigen** and LbeIF-4A and LmeIF-4A)

IT Parasitic worm
(infection; **vaccine** comprising or DNA **vaccine** encoding **antigen** or **tumor antigen** and LbeIF-4A and LmeIF-4A)

IT Biodegradable materials
(**microspheres**; **vaccine** comprising or DNA **vaccine** encoding **antigen** or **tumor antigen** and LbeIF-4A and LmeIF-4A)

IT Antibodies
RL: BPN (Biosynthetic preparation); BPR (Biological process); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(monoclonal; **vaccine** comprising or DNA **vaccine** encoding **antigen** or **tumor antigen** and LbeIF-4A and LmeIF-4A)

IT Mononuclear cell (leukocyte)
(peripheral blood; **vaccine** comprising or DNA **vaccine** encoding **antigen** or **tumor antigen** and LbeIF-4A and LmeIF-4A)

IT Blood
(peripheral; **vaccine** comprising or DNA **vaccine** encoding **antigen** or **tumor antigen** and LbeIF-4A and LmeIF-4A)

IT Interleukin 4
Interleukin 5
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(redn. of Th2-assocd. cytokines; **vaccine** comprising or DNA **vaccine** encoding **antigen** or **tumor antigen** and LbeIF-4A and LmeIF-4A)

IT **Antigens**
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**tumor**-assocd.; **vaccine** comprising or DNA **vaccine** encoding **antigen** or **tumor antigen** and LbeIF-4A and LmeIF-4A)

IT Allergy
Asthma
B cell (lymphocyte)
Chemotherapy
Dendritic cell
Drugs

Leishmania
Leishmania braziliensis
Leishmania major
Molecular cloning
Monocyte
Protein sequences
Vaccines
Virus vectors
(**vaccine** comprising or DNA **vaccine** encoding **antigen** or **tumor antigen** and LbeIF-4A and LmeIF-4A)

IT Interleukin 10
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(**vaccine** comprising or DNA **vaccine** encoding **antigen** or **tumor antigen** and LbeIF-4A and LmeIF-4A)

IT **Tumor** necrosis factors
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); USES (Uses)
(**vaccine** comprising or DNA **vaccine** encoding **antigen** or **tumor antigen** and LbeIF-4A and LmeIF-4A)

IT **Antigens**
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**vaccine** comprising or DNA **vaccine** encoding **antigen** or **tumor antigen** and LbeIF-4A and LmeIF-4A)

IT DNA
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**vaccine** comprising or DNA **vaccine** encoding **antigen** or **tumor antigen** and LbeIF-4A and LmeIF-4A)

IT Nucleic acids
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**vaccine** comprising or DNA **vaccine** encoding **antigen** or **tumor antigen** and LbeIF-4A and LmeIF-4A)

IT **Antitumor agents**
(**vaccine**; **vaccine** comprising or DNA **vaccine** encoding **antigen** or **tumor antigen** and LbeIF-4A and LmeIF-4A)

IT **Interferons**
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); USES (Uses)
(.**gamma.**; **vaccine** comprising or DNA **vaccine** encoding **antigen** or **tumor antigen** and

LbeIF-4A and LmeIF-4A)
IT 163482-21-1 186004-89-7
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study);
USES
(Uses)
(**vaccine** comprising or DNA **vaccine** encoding
antigen or **tumor antigen** and LbeIF-4A and
LmeIF-4A)

L18 ANSWER 11 OF 18 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:271490 HCAPLUS
DOCUMENT NUMBER: 130:295537
TITLE: Agonist and antagonist peptides of carcinoembryonic antigen (CEA)
INVENTOR(S): Schlom, Jeffrey; Barzaga, Elene; Zaremba, Sam
PATENT ASSIGNEE(S): United States Department of Health and Human Services,
USA
SOURCE: PCT Int. Appl., 72 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9919478	A1	19990422	WO 1998-US19794	19980922
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9895004	A1	19990503	AU 1998-95004	19980922
EP 1017810	A1	20000712	EP 1998-948429	19980922
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

PRIORITY APPLN. INFO.: US 1997-61589 P 19971010
WO 1998-US19794 W 19980922

IC ICM C12N015-12
ICS C07K014-705; A61K038-17; A61K047-00; A61K035-14; A61K048-00
CC 15-2 (Immunochemistry)
Section cross-reference(s): 1
IT Adjuvants (immunological)
Antibiotics
Antiviral agents
Bladder carcinoma inhibitors
Breast carcinoma inhibitors
Carcinoma inhibitors
Chemotherapy
Cytotoxic T cell
Fungicides
Gene therapy

Immunostimulants
Immunosuppressants
Liposomes (drug delivery systems)
Lung carcinoma inhibitors
Ovarian carcinoma inhibitors
Plasmid vectors
Prostatic carcinoma inhibitors
Virus vectors
(agonist and antagonist peptides of carcinoembryonic antigen CEA)

IT **Antitumor agents**
(digestive system; agonist and antagonist peptides of carcinoembryonic antigen CEA)

IT CD80 (antigen)
ICAM-1 (cell adhesion molecule)
Interferon .gamma.
Interleukin 12
Interleukin 2
Interleukin 6
LFA-3 (antigen)
Tumor necrosis factor .alpha.
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(immunostimulator co-treatment; agonist and antagonist peptides of carcinoembryonic **antigen** CEA)

IT Avipoxvirus
Baculoviridae
Bovine papillomavirus
Capripoxvirus
Human adenovirus
Listeria
Orthopoxvirus
Suipoxvirus
Vaccinia virus
(vector; agonist and antagonist peptides of carcinoembryonic antigen CEA)

REFERENCE COUNT: 6
REFERENCE(S):
(1) Chen, Y; THE JOURNAL OF IMMUNOLOGY 1996, V157, P3783 HCAPLUS
(2) Jameson, S; IMMUNITY 1995, V2(1), P1 HCAPLUS
(3) Panicali; WO 9626271 A 1996 HCAPLUS
(4) Schlom, J; WO 9219266 A 1992 HCAPLUS
(5) Tsang, K; JOURNAL OF THE NATIONAL CANCER INSTITUTE 1995, V87(13), P982 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 12 OF 18 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:175585 HCAPLUS
DOCUMENT NUMBER: 130:222113
TITLE: cDNA sequence of Leishmania major homolog of the eukaryotic initiation factor 4A (LmeIF4A) **antigen**, and its use in enhancing immune responses to **tumor antigens**, DNA **vaccines** or other **antigens**
INVENTOR(S): Reed, Steven G.
PATENT ASSIGNEE(S): Corixa Corporation, USA
SOURCE: U.S., 44 pp., Cont.-in-part of U.S. Ser. No. 607,509.
CODEN: USXXAM

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 7
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5879687	A	19990309	US 1996-634642	19960418
US 5876735	A	19990302	US 1996-607509	19960223
CA 2223421	AA	19961212	CA 1996-2223421	19960605
WO 9639524	A1	19961212	WO 1996-US9141	19960605
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN				
AU 9659880	A1	19961224	AU 1996-59880	19960605
EP 832236	A1	19980401	EP 1996-917229	19960605
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
CN 1194000	A	19980923	CN 1996-195382	19960605
BR 9608898	A	19990629	BR 1996-8898	19960605
JP 2001503014	T2	20010306	JP 1997-501532	19960605
NO 9705730	A	19980205	NO 1997-5730	19971205
US 6013268	A	20000111	US 1997-989370	19971212

PRIORITY APPLN. INFO.:

US 1994-232534	B2	19940422
US 1995-488386	B2	19950606
US 1996-607509	A2	19960223
US 1995-454036	A2	19950530
US 1996-634642	A	19960418
WO 1996-US9141	W	19960605

IC ICM A61K039-008
ICS A61K039-39; C07K014-44; C12N015-30
NCL 424269100
CC 15-2 (Immunochemistry)
Section cross-reference(s): 1, 3, 10, 14
ST cDNA sequence Leishmania LmeIF4A **antigen** homolog eIF4A; DNA sequence Leishmania LbeIF4A **antigen** homolog eIF4A; LmeIF4A **antigen** enhancement immune response **tumor vaccine**; LbeIF4A **antigen** immunostimulant cytokine secretion mRNA expression Leishmania; cell mediated humoral immunity enhancement Leishmania LmeIF4A LbeIF4A
IT **Tumor** necrosis factor .alpha.
RL: BOC (Biological occurrence); BPR (Biological process); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(DNA sequence of Leishmania braziliensis homolog of the eukaryotic initiation factor 4A (LbeIF4A **antigen**) gene, and its use in stimulating and enhancing immune responses)
IT **Interferon .gamma.**
Interleukin 12
RL: BOC (Biological occurrence); BPR (Biological process); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); OCCU (Occurrence); PROC (Process)
(DNA sequence of Leishmania braziliensis homolog of the eukaryotic initiation factor 4A (LbeIF4A antigen) gene, and its use in stimulating

and enhancing immune responses)

IT **Vaccines**
(DNA; cDNA sequence of Leishmania major homolog of the eukaryotic initiation factor 4A (LmeIF4A **antigen**), and its use in enhancing immune responses to **tumor antigens**, DNA **vaccines** or other **antigens**)

IT Initiation factor eIF-4
RL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); BUU (Biological use, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(LbeIF4A and LmeIF4a; enhancement of immune responses to **tumor antigens**, DNA **vaccines**, or other **antigens** using Leishmania eukaryotic initiation factor 4A (LbeIF4A and LmeIF4A **antigens**) homologs)

IT **Antigens**
RL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); BUU (Biological use, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(LmeIF4a; cDNA sequence of Leishmania major homolog of the eukaryotic initiation factor 4A (LmeIF4A **antigen**), and its use in enhancing immune responses to **tumor antigens**, DNA **vaccines** or other **antigens**)

IT Antibodies
RL: MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative)
(anti-trinitrophenol and ant-MUC-1 antibodies; cDNA sequence of Leishmania major homolog of the eukaryotic initiation factor 4A (LmeIF4A **antigen**), and its use in enhancing immune responses to **tumor antigens**, DNA **vaccines** or other **antigens**)

IT **Microspheres**
(biodegradable; cDNA sequence of Leishmania major homolog of the eukaryotic initiation factor 4A (LmeIF4A **antigen**), and its use in enhancing immune responses to **tumor antigens**, DNA **vaccines** or other **antigens**)

IT **Antitumor agents**
Leishmania major
Molecular cloning
(cDNA sequence of Leishmania major homolog of the eukaryotic initiation factor 4A (LmeIF4A **antigen**), and its use in enhancing immune responses to **tumor antigens**, DNA **vaccines** or other **antigens**)

IT Cell-mediated immunity
Humoral immunity
(enhancement of immune responses to **tumor antigens**, DNA **vaccines**, or other **antigens** using Leishmania eukaryotic initiation factor 4A (LbeIF4A and LmeIF4A **antigens**) homologs)

IT mRNA
RL: BOC (Biological occurrence); BPR (Biological process); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(of **IFN-.gamma.**, IL-2, IL-4 and IL-10 genes; DNA sequence of Leishmania braziliensis homolog of the eukaryotic initiation factor 4A (LbeIF4A antigen) gene, and its use in stimulating

and enhancing immune responses)
IT cDNA sequences
(of Leishmania major homolog of the eukaryotic initiation factor 4A (LmeIF4A **antigen**), and its use in enhancing immune responses to **tumor antigens**, DNA **vaccines** or other **antigens**)
IT Cytotoxic T cell
(response against ovalbumin; cDNA sequence of Leishmania major homolog of the eukaryotic initiation factor 4A (LmeIF4A **antigen**), and its use in enhancing immune responses to **tumor antigens**, DNA **vaccines** or other **antigens**)
IT **Antigens**
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(**tumor**-specific **antigens**; cDNA sequence of Leishmania major homolog of the eukaryotic initiation factor 4A (LmeIF4A **antigen**), and its use in enhancing immune responses to **tumor antigens**, DNA **vaccines** or other **antigens**)
IT 186004-89-7P 186004-91-1P
RL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); BUU (Biological use, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(amino acid sequence; of Leishmania major homolog of the eukaryotic initiation factor 4A (LmeIF4A **antigen**), and its use in enhancing immune responses to **tumor antigens**, DNA **vaccines** or other **antigens**)
IT 186004-90-0
RL: BUU (Biological use, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(nucleotide sequence; cDNA sequence of Leishmania major homolog of the eukaryotic initiation factor 4A (LmeIF4A **antigen**), and its use in enhancing immune responses to **tumor antigens**, DNA **vaccines** or other **antigens**)
REFERENCE COUNT: 18
REFERENCE(S): (1) Afonso, L; Science 1994, V263, P235 HCAPLUS
(2) Anon; WO 9529239 1995 HCAPLUS
(3) Anon; WO 9639524 1996 HCAPLUS
(4) Carvalho; J Immunol 1994, V152, P5949 HCAPLUS
(5) Ghalib; J Immunol 1995, V154(9), P4623 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 13 OF 18 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:147258 HCAPLUS
DOCUMENT NUMBER: 130:218285
TITLE: Methods for enhancement of protective immune responses
INVENTOR(S): Reed, Steven G.
PATENT ASSIGNEE(S): Corixa Corporation, USA
SOURCE: U.S., 45 pp., Cont.-in-part of U.S. Ser. No. 488,386, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 7
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5876735	A	19990302	US 1996-607509	19960223
US 5879687	A	19990309	US 1996-634642	19960418
CA 2223421	AA	19961212	CA 1996-2223421	19960605
WO 9639524	A1	19961212	WO 1996-US9141	19960605
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN				
AU 9659880	A1	19961224	AU 1996-59880	19960605
EP 832236	A1	19980401	EP 1996-917229	19960605
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
CN 1194000	A	19980923	CN 1996-195382	19960605
BR 9608898	A	19990629	BR 1996-8898	19960605
JP 2001503014	T2	20010306	JP 1997-501532	19960605
NO 9705730	A	19980205	NO 1997-5730	19971205
US 6013268	A	20000111	US 1997-989370	19971212
PRIORITY APPLN. INFO.:			US 1994-232534 B2	19940422
			US 1995-488386 B2	19950606
			US 1995-454036 A2	19950530
			US 1996-607509 A2	19960223
			US 1996-634642 A	19960418
			WO 1996-US9141 W	19960605

IC ICM A61K039-00
ICS A61K039-002; A61K039-008; A61K009-127
NCL 424269100
CC 1-7 (Pharmacology)
Section cross-reference(s): 15
IT **Antitumor agents**
Cytotoxic lymphocyte
DNA-DNA hybridization
Immunostimulants
Leishmania braziliensis
Leishmania major
Microencapsulation
Molecular cloning
Mononuclear cell (leukocyte)
Protein sequences
Th1 cell
cDNA sequences
(Leishmania homologs of eukaryotic initiation factor 4A for enhancement
of **antitumor** immune responses)
IT **Interferon .gamma.**
Tumor necrosis factor .alpha.
RL: BOC (Biological occurrence); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); OCCU (Occurrence)
(Leishmania homologs of eukaryotic initiation factor 4A for enhancement
of antitumor immune responses)
IT Cytokines
Tumor-associated **antigen**

RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(Leishmania homologs of eukaryotic initiation factor 4A for enhancement
of antitumor immune responses)
IT **Microspheres** (drug delivery systems)
(biodegradable; Leishmania homologs of eukaryotic initiation factor 4A for enhancement of antitumor immune responses)
REFERENCE COUNT: 16
REFERENCE(S): (1) Afonso, L; Science 1994, V263, P235 HCAPLUS
(3) Ghalib; J Immunol 1995, V154(9), P4623 HCAPLUS
(4) Heinzel; J Exp Med 1993, V177, P1505 HCAPLUS
(5) Heinzel, F; J Exp Med 1993, V177(5), P1505 HCAPLUS
(6) Kim; Nuc Acids Res 1993, V21(8), P2012 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 14 OF 18 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:141869 HCAPLUS
DOCUMENT NUMBER: 130:351077
TITLE: Presentation of renal **tumor antigens** by human dendritic cells activates **tumor**-infiltrating lymphocytes against autologous **tumor**: Implications for live kidney cancer **vaccines**
AUTHOR(S): Mulders, Peter; Tso, Cho-Lea; Gitlitz, Barbara; Kaboo, Randhir; Hinkel, Andreas; Frand, Stacey; Kiertscher, Sylvia; Roth, Michael D.; DeKernion, Jean; Figlin, Robert; Belldegrun, Arie
CORPORATE SOURCE: Immunotherapy Laboratory, Department of Urology, University of California at Los Angeles, Los Angeles, CA, 90095-1738, USA
SOURCE: Clin. Cancer Res. (1999), 5(2), 445-454
CODEN: CCREF4; ISSN: 1078-0432
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English
CC 15-8 (Immunochemistry)
ST renal carcinoma **antigen** dendritic cell **tumor** infiltrating lymphocyte
IT **Interferon .gamma.**
Interleukin 6
Tumor necrosis factor .alpha.
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(cytokine gene expression by dendritic cell-activated tumor-infiltrating lymphocytes of humans with renal cell carcinoma)
IT **Vaccines**
(cytokine-induced human dendritic cells activate tumor-infiltrating lymphocytes against autologous renal cell carcinoma in relation to)
IT **Liposomes**
(for delivery of **tumor antigens** to cytokine-induced dendritic cells in humans with renal cell carcinoma)
IT Class I HLA **antigens**
HLA-DR **antigen**
RL: BOC (Biological occurrence); BIOL (Biological study); OCCU (Occurrence)

(**liposomal** delivery of **tumor antigens** enhances dendritic cell expression of)

REFERENCE COUNT: 41

REFERENCE(S):
(2) Applegate, K; Cancer Res 1990, V50, P7153 HCAPLUS
(6) Bender, A; J Immunol Methods 1996, V196, P121 HCAPLUS
(7) Bonham, C; Transplant Immunol 1996, V4, P186 HCAPLUS
(8) Cella, M; J Exp Med 1996, V184, P747 HCAPLUS
(10) Chaux, P; Lab Invest 1996, V74, P975 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 15 OF 18 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:81592 HCAPLUS
DOCUMENT NUMBER: 130:138306
TITLE: Cellular vesicles (texosomes and dexosomes), preparation, and use in immune stimulation
INVENTOR(S): Zitvogel, Laurence; Raposo, Graca; Regnault, Armelle; Amigorena, Sebastian
PATENT ASSIGNEE(S): Institut National De La Sante Et De La Recherche Medicale, Fr.; Institut Gustave Roussy; Centre National De La Recherche Scientifique; Institut Curie
SOURCE: PCT Int. Appl., 98 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9903499	A1	19990128	WO 1998-FR1431	19980703
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
FR 2766205	A1	19990122	FR 1997-9007	19970716
FR 2774697	A1	19990813	FR 1998-1437	19980206
AU 9884464	A1	19990210	AU 1998-84464	19980703
EP 1001806	A1	20000524	EP 1998-935097	19980703
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2000512161	T2	20000919	JP 1999-506548	19980703

PRIORITY APPLN. INFO.:
FR 1997-9007 A 19970716
FR 1998-1437 A 19980206
WO 1998-FR1431 W 19980703

IC ICM A61K039-00
ICS A61K039-12; C12N005-08
CC 15-10 (Immunochemistry)
Section cross-reference(s): 63
IT Adjuvants (immunological)
Anti-infective agents

Antigen-presenting cell
Antitumor agents
B cell (lymphocyte)
Breast carcinoma inhibitors
CD8-positive T cell
Cytotoxic T cell
Drug delivery systems
Endosome
Immunomodulators
Immunostimulants
Immunotherapy
Liposomes
Membranes (biological)
Parasiticides
T cell (lymphocyte)
Tissue culture (animal)
(cellular vesicles (texosomes and dexosomes), prepn., and use in immune
stimulation)
IT CD86 (antigen)
Cell adhesion molecules
Class I MHC antigens
Class II MHC antigens
HLA-A2 antigen
Hormones (animal), biological studies
Nucleic acids
Protein HSP70
Tumor-associated **antigen**
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(cellular vesicles (texosomes and dexosomes), prepn., and use in immune
stimulation)
IT **Interferon .gamma.**
RL: BPR (Biological process); BUU (Biological use, unclassified); BIOL (Biological study); PROC (Process); USES (Uses)
(cellular vesicles (texosomes and dexosomes), prepn., and use in immune
stimulation)
IT **Antitumor agents**
(mastocytoma inhibitors; cellular vesicles (texosomes and dexosomes), prepn., and use in immune stimulation)
REFERENCE COUNT: 10
REFERENCE(S): (1) Amigorena; Nature 1994, V369, P113 HCAPLUS
(2) Bernhard; Cancer Research 1995, V55, P1099 HCAPLUS
(3) Gruenberg; The Journal of Cell Biology 1989, V108, P1301 HCAPLUS
(4) Hsu, F; Nature Medicine 1996, V2(1), P52 HCAPLUS
(5) Raposo; Journal of Experimental Medicine 1996, V183, P1161 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 16 OF 18 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1998:542986 HCAPLUS
DOCUMENT NUMBER: 129:166180
TITLE: pH-sensitive **liposomes** and other types of

encapsulated **vaccines** containing immunomodulators, and methods for making and using same
INVENTOR(S): Bystryn, Jean-Claude
PATENT ASSIGNEE(S): USA
SOURCE: PCT Int. Appl., 72 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9833520	A1	19980806	WO 1998-US2463	19980205
W: JP, US				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
EP 983086	A1	20000308	EP 1998-906248	19980205
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

PRIORITY APPLN. INFO.: US 1997-37217 19970205
WO 1998-US2463 19980205

IC ICM A61K039-00
ICS A61K039-02; A61K039-12; A61K045-05; A61K047-42; A61K047-44; A61K009-127; G01N033-53; G01N033-543; G01N033-567
CC 63-3 (Pharmaceuticals)
Section cross-reference(s): 15
ST **vaccine liposome** immunostimulant formulation pH
IT T cell (lymphocyte)
(CD8-pos.; pH-sensitive **liposomes** and other types of encapsulated **vaccines** contg. immunomodulators)
IT CD8 (antigen)
RL: BOC (Biological occurrence); BIOL (Biological study); OCCU (Occurrence)
(T-cell bearing; pH-sensitive **liposomes** and other types of encapsulated **vaccines** contg. immunomodulators)
IT Heat-shock proteins
Toxins
RL: DEV (Device component use); USES (Uses)
(antigen carriers; pH-sensitive **liposomes** and other types of encapsulated **vaccines** contg. immunomodulators)
IT Brain tumors
Breast tumors
Colon tumors
Digestive system tumors
Gastric tumors
Leukemia
Lung tumors
Ovarian tumors
Prostatic tumors
(antigens of; pH-sensitive **liposomes** and other types of encapsulated **vaccines** contg. immunomodulators)
IT Biodegradable polymers
RL: DEV (Device component use); USES (Uses)
(beads; pH-sensitive **liposomes** and other types of encapsulated **vaccines** contg. immunomodulators)

IT Antibodies
RL: BPR (Biological process); DEV (Device component use); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(cytokine-specific; pH-sensitive **liposomes** and other types of encapsulated **vaccines** contg. immunomodulators)
IT Antigens
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); PEP (Physical, engineering or chemical process); BIOL (Biological study); PROC (Process)
(delivery and presentation of; pH-sensitive **liposomes** and other types of encapsulated **vaccines** contg. immunomodulators)
IT Bacteria (Eubacteria)
Fungi
Mycoplasma
Prion
Virus
(immunity to; pH-sensitive **liposomes** and other types of encapsulated **vaccines** contg. immunomodulators)
IT Fluoropolymers, uses
RL: DEV (Device component use); USES (Uses)
(membrane; pH-sensitive **liposomes** and other types of encapsulated **vaccines** contg. immunomodulators)
IT Endocytosis
(of antigen; pH-sensitive **liposomes** and other types of encapsulated **vaccines** contg. immunomodulators)
IT Antigen presentation
Autoimmune diseases
Drug carriers (drug delivery systems)
Immunostimulants
Liposomes (drug delivery systems)
Microencapsulation
Vaccines
pH
(pH-sensitive **liposomes** and other types of encapsulated **vaccines** contg. immunomodulators)
IT Interleukin 1
Interleukin 12
Interleukin 2
Interleukin 4
Interleukin 6
Melanoma-associated antigen
RL: BAC (Biological activity or effector, except adverse); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(pH-sensitive **liposomes** and other types of encapsulated **vaccines** contg. immunomodulators)
IT **Interferon .gamma.**
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pH-sensitive **liposomes** and other types of encapsulated **vaccines** contg. immunomodulators)
IT CD4 (antigen)
Class I MHC antigens
Class II HLA antigens
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)

(pH-sensitive **liposomes** and other types of encapsulated **vaccines** contg. immunomodulators)
IT Glass beads
RL: DEV (Device component use); USES (Uses)
(pH-sensitive **liposomes** and other types of encapsulated **vaccines** contg. immunomodulators)
IT **Antigens**
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(**tumor**-specific **antigens**; pH-sensitive **liposomes** and other types of encapsulated **vaccines** contg. immunomodulators)
IT Organelle
(virosome; pH-sensitive **liposomes** and other types of encapsulated **vaccines** contg. immunomodulators)
IT 7439-89-6, Iron, uses
RL: DEV (Device component use); USES (Uses)
(beads; pH-sensitive **liposomes** and other types of encapsulated **vaccines** contg. immunomodulators)
IT 24937-79-9, Immobilon-p
RL: DEV (Device component use); USES (Uses)
(membrane; pH-sensitive **liposomes** and other types of encapsulated **vaccines** contg. immunomodulators)
IT 83869-56-1, Gmcsf
RL: BAC (Biological activity or effector, except adverse); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(pH-sensitive **liposomes** and other types of encapsulated **vaccines** contg. immunomodulators)
IT 1510-21-0, Cholesteryl hemisuccinate 2462-63-7, Dope
RL: DEV (Device component use); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(pH-sensitive **liposomes** and other types of encapsulated **vaccines** contg. immunomodulators)
IT 25104-18-1, Polylysine 38000-06-5, Polylysine
RL: MOA (Modifier or additive use); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(pH-sensitive **liposomes** and other types of encapsulated **vaccines** contg. immunomodulators)

L18 ANSWER 17 OF 18 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1997:776264 HCAPLUS
DOCUMENT NUMBER: 128:60724
TITLE: Monoclonal antibody H11 to C-**antigen** : **tumor** imaging, diagnosis, and therapy
INVENTOR(S): Dan, Michael D.; Maiti, Pradip K.; Kaplan, Howard A.
PATENT ASSIGNEE(S): Novopharm Biotech, Inc., USA; Dan, Michael D.; Maiti, Pradip K.; Kaplan, Howard A.
SOURCE: PCT Int. Appl., 125 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9744461	A2	19971127	WO 1997-US8962	19970522
WO 9744461	A3	19980507		
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2255540	AA	19971127	CA 1997-2255540	19970522
AU 9733696	A1	19971209	AU 1997-33696	19970522
AU 725238	B2	20001012		
EP 912738	A2	19990506	EP 1997-929703	19970522
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
BR 9710811	A	19990817	BR 1997-10811	19970522
CN 1229436	A	19990922	CN 1997-194815	19970522
JP 2000511421	T2	20000905	JP 1997-542853	19970522
NO 9805150	A	19990120	NO 1998-5150	19981104

PRIORITY APPLN. INFO.: US 1996-657449 A2 19960522
WO 1997-US8962 W 19970522

IC ICM C12N015-13
ICS A61K039-395; A61K047-48; A61K051-10; C07K016-30; C12N015-86; C12N005-10; A61K039-00

CC 15-3 (Immunochemistry)
Section cross-reference(s): 1, 3, 8

IT **Antigens**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(C-; monoclonal antibody H11 to C-**antigen** for **tumor** imaging, diagnosis, and therapy)

IT Monoclonal IgM
RL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); PRP (Properties); PUR (Purification or recovery); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(H11; monoclonal antibody H11 to C-**antigen** for **tumor** imaging, diagnosis, and therapy)

IT Ribosome-inactivating proteins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(PAP (pokeweed antiviral protein), with anti-C-**antigen** antibody; for **tumor** therapy)

IT Breast carcinoma inhibitors
Prostatic carcinoma inhibitors
(adenocarcinoma; monoclonal antibody H11 to C-**antigen** for **tumor** imaging, diagnosis, and therapy)

IT Synthetic genes
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(animal; monoclonal antibody H11 to C-**antigen** for **tumor** imaging, diagnosis, and therapy)

IT Adenocarcinoma inhibitors

(breast; monoclonal antibody H11 to C-**antigen** for **tumor** imaging, diagnosis, and therapy)

IT Radionuclides
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(conjugates, with anti-C-**antigen** antibody; for **tumor** imaging and anti-neoplastic activity)

IT Fluorescent substances
Luminescent substances
(conjugates, with anti-C-**antigen** antibody; for **tumor** therapy)

IT Ricins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(conjugates, with anti-C-**antigen** antibody; for **tumor** therapy)

IT Enzymes, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(conjugates, with anti-C-**antigen** antibody; monoclonal antibody H11 to C-**antigen** for **tumor** imaging, diagnosis, and therapy)

IT **Interferon .gamma.**
Interleukin 12
Interleukin 2
Interleukin 4
Tumor necrosis factors
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(fusion products, with anti-C-**antigen** antibody fragments; for **tumor** therapy)

IT Immunoglobulin fragments
RL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); PRP (Properties); PUR (Purification or recovery); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(fusion products, with biol. response modifiers; monoclonal antibody H11 to C-**antigen** for **tumor** imaging, diagnosis, and therapy)

IT Breast adenocarcinoma
(inhibitors; monoclonal antibody H11 to C-**antigen** for **tumor** imaging, diagnosis, and therapy)

IT **Antitumor agents**
Bladder carcinoma inhibitors
Colon adenocarcinoma inhibitors
Genetic vectors
Glioma inhibitors
Immunodiagnosis
Immunoscintigraphy
Immunotherapy
Injections (drug delivery systems)
Liposomes (drug delivery systems)
Melanoma inhibitors
Neuroblastoma inhibitors
Plasmid vectors
Sarcoma inhibitors
Small-cell carcinoma inhibitors (lung)
Vaccinia virus
Virus vectors
(monoclonal antibody H11 to C-**antigen** for **tumor** imaging, diagnosis, and therapy)

IT Chimeric antibodies
Humanized antibodies
Single chain antibodies
RL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); PRP (Properties); PUR (Purification or recovery); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(monoclonal antibody H11 to C-**antigen** for **tumor** imaging, diagnosis, and therapy)

IT Adenocarcinoma inhibitors
(prostatic; monoclonal antibody H11 to C-**antigen** for **tumor** imaging, diagnosis, and therapy)

IT Genes (animal)
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(synthetic; monoclonal antibody H11 to C-**antigen** for **tumor** imaging, diagnosis, and therapy)

IT Alkaloids, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(vinca, with anti-C-**antigen** antibody; for **tumor** therapy)

IT Exotoxin A
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(with anti-C-**antigen** antibody; for **tumor** therapy)

IT 200298-77-7 200298-79-9 200298-81-3 200298-83-5
RL: PRP (Properties)
(amino acid sequence; monoclonal antibody H11 to C-**antigen** for **tumor** imaging, diagnosis, and therapy)

IT 50-18-0D, Cyclophosphamide, anti-C-**antigen** antibody conjugates
50-44-2D, Mercaptopurine, anti-C-**antigen** antibody conjugates
50-76-0D, Dactinomycin, anti-C-**antigen** antibody conjugates
51-21-8D, Fluorouracil, anti-C-**antigen** antibody conjugates
53-19-0D, Mitotane, anti-C-**antigen** antibody conjugates
54-91-1D, Pipobroman, anti-C-**antigen** antibody conjugates
55-86-7D, anti-C-**antigen** antibody conjugates 59-05-2D, Methotrexate, anti-C-**antigen** antibody conjugates 66-75-1D, Uracil mustard, anti-C-**antigen** antibody conjugates 143-67-9D, Vinblastine sulfate, anti-C-**antigen** antibody conjugates
147-94-4D, Cytarabine, anti-C-**antigen** antibody conjugates
148-82-3D, Melphalan, anti-C-**antigen** antibody conjugates
154-42-7D, Thioguanine, anti-C-**antigen** antibody conjugates
366-70-1D, Procarbazine hydrochloride, anti-C-**antigen** antibody conjugates 1404-00-8D, Mitomycin, anti-C-**antigen** antibody conjugates 1406-72-0D, Restrictocin, anti-C-**antigen** antibody conjugates 2068-78-2D, Vincristine sulfate, anti-C-**antigen** antibody conjugates 4342-03-4D, Dacarbazine, anti-C-**antigen** antibody conjugates 9013-93-8D, Phospholipase, anti-C-**antigen** antibody conjugates 9041-93-4D, Bleomycin sulfate, anti-C-**antigen** antibody conjugates 13010-47-4D, Lomustine, anti-C-**antigen** antibody conjugates 15663-27-1D, Cisplatin, anti-C-**antigen** antibody conjugates 18883-66-4D, Streptozotocin, anti-C-**antigen** antibody conjugates 23541-50-6D, Daunorubicin hydrochloride, anti-C-**antigen** antibody conjugates 25316-40-9D, Adriamycin, anti-C-**antigen** antibody conjugates 33069-62-4D, Taxol, anti-C-**antigen** antibody conjugates 33419-42-0D, Etoposide, anti-C-**antigen** antibody conjugates 41575-94-4D, Carboplatin, anti-C-**antigen** antibody conjugates 53910-25-1D,

Pentostatin, anti-C-**antigen** antibody conjugates 59917-39-4D, Vindesine sulfate, anti-C-**antigen** antibody conjugates 83869-56-1D, GM-CSF, fusion products, with anti-C-**antigen** antibody fragments
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(for **tumor** therapy)

IT 200298-76-6 200298-78-8 200298-80-2 200298-82-4
RL: PRP (Properties)
(nucleotide sequence; monoclonal antibody H11 to C-**antigen** for **tumor** imaging, diagnosis, and therapy)

L18 ANSWER 18 OF 18 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1997:562991 HCAPLUS
DOCUMENT NUMBER: 127:219544
TITLE: **Vaccine** for B-cell malignancies
INVENTOR(S): Popescu, Mircea C.; Kwak, Larry; Ochoa, Augusto C.; Boni, Larry
PATENT ASSIGNEE(S): Biomira USA Inc., USA; Popescu, Mircea C.; Kwak, Larry; Ochoa, Augusto C.; Boni, Larry
SOURCE: PCT Int. Appl., 37 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9729769	A1	19970821	WO 1997-US2351	19970213
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9722734	A1	19970902	AU 1997-22734	19970213
EP 918539	A1	19990602	EP 1997-905966	19970213
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2000507214	T2	20000613	JP 1997-529517	19970213

PRIORITY APPLN. INFO.: US 1996-11783 P 19960216
WO 1997-US2351 W 19970213

IC ICM A61K039-00
ICS A61K039-39; A61K039-395; A61K045-05; A61K009-127
CC 15-2 (Immunochemistry)
ST B cell **tumor vaccine; antigen tumor** assocd **vaccine;** interleukin 2 B cell **vaccine; liposome** antitumor **vaccine**
IT Lymphoma inhibitors
(B cell; **vaccine** for B-cell malignancies)
IT B cell (lymphocyte)
Burkitt's lymphoma
Human herpesvirus 4
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(antigen of; **vaccine** for B-cell malignancies)
IT B cell lymphoma
(inhibitors; **vaccine** for B-cell malignancies)
IT Multiple myeloma
Plasma cell
(plasma-cell myeloma inhibitors; **vaccine** for B-cell malignancies)
IT **Antitumor agents**
(plasma-cell myeloma; **vaccine** for B-cell malignancies)
IT B cell chronic lymphocytic leukemia
Liposomes (drug delivery systems)
Vaccines
(**vaccine** for B-cell malignancies)
IT Class I HLA antigens
Class II HLA antigens
Cytokines
Glycolipids
Interferon .gamma.
Interleukin 2
Lipids, biological studies
MUC1 mucin
Phospholipids, biological studies
Tumor-associated **antigen**
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**vaccine** for B-cell malignancies)
IT 57-88-5, Cholesterol, biological studies 18656-38-7 61361-72-6, Dimyristoylphosphatidylglycerol 81627-83-0, Macrophage colony-stimulating factor 83869-56-1, Granulocyte-macrophage colony-stimulating factor
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**vaccine** for B-cell malignancies)

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=> fil wpids

FILE 'WPIDS' ENTERED AT 10:08:33 ON 23 AUG 2001
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=> d his l1-l12


     (FILE 'WPIDS' ENTERED AT 10:01:59 ON 23 AUG 2001)
               DEL HIS Y
L1         1236 S (TUMOR OR TUMOUR) (4A) ANTIGEN#
L2         1173 S GAMMA (4A) (IFN OR INTERFERON#)
L3           51 S L1 AND L2
L4           48 S L3 AND D16/DC
L5        14016 S VACCIN?
L6           32 S L3 AND L5
L7           49 S L6 OR L4
L8         8007 S LIPOSOM? OR MINIPELLET# OR MICROSPHER? OR MINI PELLET# OR
MIC
L9            8 S L7 AND L8
L10       17460 S  (SLOW OR DELAY? OR CONTROLL? OR TIME# ) (3A) RELEAS?
L11           1 S L7 AND L10
L12           8 S L9 OR L11

=> d .wp tech l12 1-18


L12  ANSWER 1 OF 8  WPIDS COPYRIGHT 2001   DERWENT INFORMATION LTD
AN   2001-432554 [46]   WPIDS
DNC  C2001-130828
TI   New synthetic bacterial lipid A analogs, useful e.g. as adjuvants to
     enhance immune responses to antigens in vaccine formulations and
     as anticancer agents.
DC   B03 B04 D16
IN   BACH, M; JIANG, Z; KOGANTY, R; LONGENECKER, M; YALAMATI, D
PA   (BIOM-N) BIOMIRA INC
CYC  94
PI   WO 2001036433 A2 20010525 (200146)* EN  118p
```

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ
NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM
DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC
LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE
SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

ADT WO 2001036433 A2 WO 2000-US31281 20001115
PRAI US 1999-164928 19991115
AB WO 200136433 A UPAB: 20010815
NOVELTY - Synthetic bacterial lipid A analogs (I) and their salts are new.

DETAILED DESCRIPTION - Synthetic bacterial lipid A analogs of formula (I) and their salts are new.

At least one of R1-R5 is OCCH2CH(CONHR')NHRCO, B(CH2)nCH(R')OA(CH2)mCH(X)R or L(CH2)nCH(R'')OB(CH2)mCH(R')OAR and the remaining R1-R5 are selected from H, R, COR, OCCH2CH(CONHR')NHRCO, B(CH2)nCH(R')OA(CH2)mCH(X)R, L(CH2)nCH(R'')OB(CH2)mCH(R')OAR, B(CH2)mCH(R')OAR and A(CH2)mCH(X)R;

R, R', R'' = H, optionally substituted and optionally saturated 1-20C aliphatic hydrocarbon;

A, B, L = CH2, CO or CS;

X = OH, SH, NH2 or halo;

m, n = 0-10;

X1, X2 = O or NH;

Y1, Y2 = OH, OP(O)(OH)2, COOH, OSO3H, CH(COOH)2 or OP(O)(OH)OCH2CH2NH2;

Z = H, CH2E or CH2MG;

E = H, halo, OH, NH2, OSO3H, SO3H, P(O)(OH)2 or OP(O)(OH)2;

M = O, S, OC(O), SC(O), OC(S) or NHC(O);

G = H or optionally substituted and optionally saturated 1-20C aliphatic hydrocarbon.

INDEPENDENT CLAIMS are also included for the following:

(1) compounds (I) in which R1 = R4 = R5 and R1-R5 are selected from R, COR, OCCH2CH(CONHR')NHRCO, B(CH2)nCH(R')OA(CH2)mCH(X)R, L(CH2)nCH(R'')OB(CH2)mCH(R')OAR, B(CH2)mCH(R')OAR and A(CH2)mCH(X)R;

(2) compounds of formula (II);

R1II, R2II = C(O)CH2CH(NHRCO) or L'(CH2)nCH(R'')OB'(CH2)mCH(R')OA'R;

A', B', L' = CH2 or CO;

(3) specific synthetic lipid acids of formula (IIIa) and (III'a);

(4) compounds of formula (IV)-(VII);

R1IV, R1V = benzyloxy, allyloxy, OH or OC(NH)CCl3;

R2IV , R2V= H, COOCH2CCl3 or OCCH2CH(NHCO(CH2)n'Me)CONH(CH2)m'Me;

m', n', x, y, z = 0-20;

R3IV, R3V = CO(CH2)zMe or COCH2CH((CH2)yMe)OA'(CH2)xMe;

R4V = H or P(O)(OBn)2;

R1VI = amino, phthalamido or NHCOCH2CH((CH2)yMe)OA'(CH2)xMe;

R2VI = allyl or benzyl;

R1VII = H, COOCH2CCl3, a group of formula (a) or C(O)CH2CH(OA'(CH2)xMe)(CH2)yMe;

R2VII = C(O)CH2CH(OD)(CH2)xMe;

D = benzyl, (CH2)zMe or CO(CH2)yMe;

(5) compounds of formula (VIII)-(X);

R1VIII, R4VIII, R1IX, R4IX = C(O)CH2CH(OA'(CH2)xMe)(CH2)yMe;

R2VIII, R2IX = H, allyl, benzyl or C(O)CH2CH(OBn)(CH2)zMe;

R3VIII, R3IX = H, COOCH2CCl3, OCCH2CH(NHCO(CH2)n'Me)CONH(CH2)m'Me or

C(O)CH2CH(OA'(CH2)xMe)(CH2)yMe;
R5IX = H or P(O)(OBn)2;
R1X = C(O)CH2CH(OA'(CH2)xMe)(CH2)yMe or group (a);
R2X = benzyl or C(O)CH2CH(OBn)(CH2)zMe;
R3X = H, COOCH2CCl3, C(O)CH2CH(OBn)(CH2)zMe or
C(O)CH2CH(OA'(CH2)xMe)(CH2)yMe;
R4X = C(O)CH2CH(OA'(CH2)xMe)(CH2)yMe;

(6) introducing a phosphate group into the 4-O-position of a hexopyranose derivative;

(7) a non-naturally occurring liposome whose membrane comprises: (a) any of the above compounds; and (b) at least one epitope;

(8) a pharmaceutical composition comprising a liposome as in (7), the composition comprising a vaccinologically effective amount of the antigen;

(9) use of the liposome in (7) in the manufacture of a composition for the prevention or treatment of a disease preventable or treatable by eliciting an immune response to the antigen.

ACTIVITY - Immunostimulant; antibacterial; cytostatic.

MECHANISM OF ACTION - Lipid A biosynthesis inhibitor; antagonists for the toxic activity of lipid-A.

USE - As mono- and disaccharide based mimics of bacterial lipid A having e.g. one phosphate group at the 4-position as opposed to natural lipid A having two phosphate groups at 1- and 4-positions. Bacterial lipid A compositions are used as adjuvant to enhance the immune responses to various antigens used in vaccine formulations. May also be used as anti-tumor agents, LPS/Lipid A antagonists, inhibitors of Lipid-A biosynthesis and as antibiotics. Also for producing liposomal formulations for treating cancer where the liposomal membrane contains the analogs and at least one B-cell or T-cell epitope.

ADVANTAGE - The synthetic bacterial lipid A analogs have much lower toxicity than natural lipid A but with adjuvant properties comparable to those of natural lipid A. The analogs are chemically defined with a single structure which facilitates their tracking and control from manufacturing to final formulation. Production of the analogs is cost effective and is easily adaptable for commercial scale up while maintaining consistency in both quality and performance (cf. natural lipid A vaccines where the natural lipid A product contains a mixture of several lipid A components with varying number of lipid chains, inconsistency in composition and performance as an adjuvant, high production costs and the difficulty in determining active ingredients in final pharmaceutical composition). Further, ester bonds linking fatty acids to the sugar moiety in natural lipid A and which are vulnerable to hydrolysis under physiological conditions leading to loss of lipid chains with consequent loss of activity as an adjuvant and reduction in shelf life of vaccine formulations, are replaced by stable ether (optionally in combination with stable ester) linkages in the analogs, which enhances stability and results in longer shelf life.

Liposome formulations were used to evaluate the adjuvant properties of synthetic lipid-A structures and the immune responses to a synthetic lipopeptide antigen BP-148 (i.e. (XIII), a modified amino acid sequence derived from tumor associated MUCI mucin). For comparison, a natural lipid

A product containing a mixture of Lipid-A analogs extracted from Salmonella bacterial cell wall was used. Liposomal formulation containing the synthetic lipopeptide antigen, BP1-148, lipid A analogs or natural lipid A were used to immunize mice to measure their response in terms of T-cell blastogenesis and interferon- gamma (IFN- gamma) production. E.g. compound (33) exhibited similar adjuvant activity compared to natural lipid-A.

Dwg.0/35

TECH UPTX: 20010815

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preferred Process: In (6), introducing a phosphate group into the 4-O-position of a hexopyranose derivative comprises: (i) regioselective reductive ring opening of a hexapyranose derivative, to give a reactive 4-O-position; and (ii) introduction of a phosphate group at the reactive 4-O-position. Preferably, step (i) comprises adding a boron reagent and an acid to a compound of formula (XI). The boron reagent is especially sodium cyanoboron hydride or a dimethyl amine borane complex and the acid is hydrochloric acid. The acid is provided in a saturated diethyl ether solution, trifluoroboron diethyl ether complex. In step (ii), the product formed in step (i) is treated with the reagents (R4O)2N(iPr)2, 1H-tetrazole, in a dry organic solvent. After step (ii), an oxidizing reagent is added to give a product of formula (XII). The oxidizing reagent is meta-chloroperbenzoic acid (m-CPBA).

X = O or NH;

RXI = optionally substituted optionally saturated 1-20C aliphatic hydrocarbon, a carbohydrate unit or any protection group;

R1XI, R2XI , R1XII, R2XII= aliphatic or aromatic group or any protection group;

R3XI = optionally substituted phenyl;

R4XII = allyl or optionally substituted benzyl or phenyl.

N.B. R1XI and R1XII are defined but do not appear in formula (XI) and (XII) respectively, or in the list of definitions.

Preparation: In a specific preparation, a 2-step phosphate group introduction was effected by reacting a compound of formula (31) with dibenzyl diisopropyl phosphoramidite to form a phosphite, followed by oxidation with m-CPBA to give a compound of formula (32) in 66% yield. Catalytic hydrogenation to remove benzyl protecting groups gives the monosaccharide lipid A analog of formula (33).

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred **Liposome**: In (7), at least one epitope is a B- or T-cell epitope. At least one epitope may also be a peptide epitope, a carbohydrate, a glycopeptide or a glycolipid epitope. At least one epitope may be derived from MUCI protein. The **antigen** is a **tumor** associated **antigen**. The epitope is provided by a peptide or a lipopeptide having an amino acid sequence of formula (XIII).

Preferred Use: In (9), the lipid A analog has an adjuvanting effect on the immune response to the antigen and the disease is cancer.

L12 ANSWER 2 OF 8 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD

AN 2001-381489 [40] WPIDS

DNC C2001-116869

TI Compositions for use in a **vaccine** for treating, e.g., breast, lung and colon cancer comprises at least one peptide that comprises an isolated epitope of a **tumor**-associated **antigen**.

DC B04 **D16**

IN CELIS, E; CHESNUT, R; FIKES, J; KEOGH, E; SETTE, A; SIDNEY, J; SOUTHWOOD, S
PA (EPIM-N) EPIMMUNE INC
CYC 94
PI WO 2001041741 A1 20010614 (200140)* EN 86p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
ADT WO 2001041741 A1 WO 2000-US34318 20001213
PRAI US 2000-583200 20000530; US 1999-170448 19991213; US 2000-543608 20000405
AB WO 200141741 A UPAB: 20010719
NOVELTY - Composition (I) comprising at least one peptide that comprises an isolated, prepared epitope consisting of a sequence selected from 25 fully defined short amino acid sequences (S1)-(S25) given in the specification is new.

DETAILED DESCRIPTION - Composition (I) comprises at least one peptide that comprises an isolated, prepared epitope consisting of a sequence selected from:

(i) (S1) VLYGPDAPTV;
(ii) (S2) YLSGANLNV;
(iii) (S3) ATVGIMIGV;
(iv) (S4) LLPENNVLSPV;
(v) (S5) KLCPVQLWV;
(vi) (S6) KLB(sic)PVQLWV;
(vii) (S7) SLPPPGTRV;
(viii) (S8) SMPPPGTRV;
(ix) (S9) KLFGSLAFV;
(x) (S10) KVFGSLAFV;
(xi) (S11) VMAGVGSPYV;
(xii) (S12) ALCRWGLLL;
(xiii) (S13) FLWGPRALV;
(xiv) (S14) HLYQGCQVV;
(xv) (S15) ILHNGAYSL;
(xvi) (S16) IMIGVLVGV;
(xvii) (S17) KIFGSLAFL;
(xviii) (S18) KVAELVHFL;
(xix) (S19) LLTFWNPPV;
(xx) (S20) LVFGIELMEV;
(xxi) (S21) QLVFGIELMEV;
(xxii) (S22) RLLQETELV;
(xxiii) (S23) VVLGVVFGI;
(xxiv) (S24) YLQLVFGIEV; and
(xxv) (S25) YMIMVKCWMI.

INDEPENDENT CLAIMS are also included for the following:

(1) a composition (II) comprising one or more peptides, and further comprising at least two epitopes selected from (S1)-(S25), where each of the one or more peptides comprise less than 50 contiguous amino acids that have 100% identity with a native peptide sequence; and

(2) a vaccine composition (III) comprising an epitope selected from (S1)-(S25) and a pharmaceutical excipient.

ACTIVITY - Cytostatic; immunomodulator.

No supporting data given.
MECHANISM OF ACTION - Vaccine (claimed); immunotherapy.
The peptides of (I) were evaluated for their potential to stimulate cytotoxic T lymphocyte (CTL) precursor responses to the tumor associated antigen (TAA)-derived peptide (in vitro primary CTL induction) and CTL recognition of tumor cells expressing the target TAA peptide epitope (recognition of endogenous targets). These criteria provided evidence that the peptides were functional epitopes.
Peripheral blood monocytic cell-derived (or bone-marrow-derived) human dendritic cells (DC), generated in vitro using granulocyte macrophage-colony stimulating factor (GM-CSF) and Interleukin-4 (IL-4) and pulsed with a peptide of interest, were used as antigen presenting cells (APCs) in primary CTL induction cultures. The peptide pulsed DC were incubated with CD8 T cells (positively selected from normal donor lymphocytes using magnetic beads) which served as the source of CTL precursors. One week after stimulation with peptide, primary cultures were tested for epitope-specific CTL activity using either a standard chromium-release assay which measures cytotoxicity or a sandwich ELISA-based interferon gamma (IFN gamma) production assay. Each of the CTL epitopes stimulated CTL induction from CD 8 T cells of normal donors.
USE - The peptide epitope compositions (I)-(II) are useful for monitoring an immune response to a tumor associated antigen or when one or more peptides are combined to create a vaccine (III) that stimulates the cellular arm of the immune system. In particular, the vaccine mediates immune responses against tumors in individuals who bear an allele of the human leukocyte antigen-A2 supertype (HLA-A2) and improve the standard of care for patients being treated for breast, colon, or lung cancer.
Dwg.0/5
TECH UPTX: 20010719
TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preparation: The peptides of the compositions may be prepared by standard recombinant techniques or synthetically on a synthesizer.
Preferred Composition: Composition (I) may comprise two or three peptides that may comprise a second or third epitope selected from (S1)-(S25), respectively. Preferably, (I) comprises eight peptides that comprise eight isolated epitopes consisting of eight sequences selected from (S1)-(S25), especially the sequences (S2), (S8), (S6), (S16), (S18), (S22), (S23), and (S24).
The epitope may be joined to an amino acid linker and admixed or joined to a cytotoxic T lymphocyte (CTL) or to a helper T cell (HTL). The HTL epitope is preferably a pan-DR binding molecule, i.e. a family of molecules that binds more than one human leukocyte antigen (HLA) class II DR molecule. The composition may further comprise a **liposome**, with the epitope on or within the **liposome**. The epitope may be joined to a lipid and may be either a homopolymer or a heteropolymer. In addition, the epitope may be bound to an HLA heavy chain, beta2-microglobulin, and streptavidin complex to form a tetramer. Furthermore, the composition may further comprise an antigen presenting cell (APC), preferably a dendritic cell, with the epitope on or within the

cell.
The composition (II) preferably has at least one peptide which comprises at least two epitopes. In addition, (II) may comprise at least 3-8 epitopes selected from (S1)-(S25). At least one of the one or more peptides is a heteropolymer or a homopolymer. Furthermore, (II) may comprise an additional epitope which may be one derived from a **tumor** associated **antigen** or a pan-DR binding molecule.
The **vaccine** (III) preferably comprises a unit dose of a peptide that comprises less than 50 contiguous amino acids that have 100% identity with a native peptide sequence of carcinoembryonic **antigen** (CEA), **tumor** associated **antigen** (HER2/neu), melanoma antigen (MAGE2 or MAGE3), or p53, where the peptide comprises an epitope selected from (S1)-(S25) and a pharmaceutical excipient. Preferably, the epitope of the **vaccine** is (S2), (S6), or (S8) and may further comprise an additional epitope such as a pan-DR binding molecule. The excipient is preferably an adjuvant and the **vaccine** may also comprise and APC.
A preferred composition or **vaccine** is, subsequently, one in which the epitope is bound to an HLA molecule on the APC, and, when an A2-restricted CTL is present, a receptor binds to a complex of the HLA molecule and the epitope.

L12 ANSWER 3 OF 8 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 2001-281839 [29] WPIDS
DNC C2001-085772
TI New **vaccine** comprising a **liposome** useful for conferring protective immunity against an intracellular pathogen.
DC B04 **D16**
IN CONLAN, J W; KRISHNAN, L; OMRI, A; PATEL, G B; SPROTT, G D
PA (CANA) NAT RES COUNCIL CANADA
CYC 93
PI WO 2001026683 A2 20010419 (200129)* EN 98p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW
AU 2000077670 A 20010423 (200147)
ADT WO 2001026683 A2 WO 2000-CA1197 20001012; AU 2000077670 A AU 2000-77670 20001012
FDT AU 2000077670 A Based on WO 200126683
PRAI US 2000-209988 20000608; US 1999-158944 19991012
AB WO 200126683 A UPAB: 20010528
NOVELTY - A **vaccine** composition comprising a **liposome** prepared from the total polar lipids extract of an archaeobacterium and an acellular antigen, preferably an isolated outer membrane from a pathogen is new.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for:
(1) eliciting an antigen-specific cytotoxic T cell response in an animal, comprising administering to the animal a **vaccine** composition comprising a **liposome** prepared from the total polar lipids extract of an archaeobacterium and an antigen, where the **liposome** serves as an immunomodulating carrier for the antigen (I);

(2) activating antigen presenting cells in an animal by upregulating costimulatory molecules B7.1 (CD80) and B7.2 (CD86) on the surface of the antigen presenting cells, comprising (I);

(3) activating CD11c+ dentritic cells in an animal, comprising administering (I) to the animal;

(4) stimulating the production of the cytokine **interferon gamma** in an animal, comprising administering (I) to the animal, where the archaeobacterium is selected from Methanobrevibacter smithii, Thermoplasma acidophilum, and Halobacterium salinarum;

(5) stimulating the production of the cytokines IL-4 and **interferon gamma** in an animal, comprising administering (I), where the extract is obtained from Methanobrevibacter smithii;

(6) stimulating the production of **tumor** necrosis factor by **antigen** presenting cells in an animal, comprising administering (I), where the extract is obtained from Methanobrevibacter smithii;

(7) recruiting Mac 1 alpha hi cells in an animal, comprising administering (I), where the **liposome** serves as an immunomodulating antigen carrier that recruits the Mac 1 alpha hi cells to the site where the **vaccine** is administered to the animal;

(8) stimulating R cell proliferation and cytokine production in an animal by activation of antigen presenting cells in the animal, comprising administering (I) to the animal;

(9) conferring to an animal protective immunity against infection by an intracellular pathogen, comprising administering (I) to the animal;

(10) immunizing an animal to confer to the animal a memory response against infection by an intracellular pathogen, comprising administering (I) to the animal;

(11) eliciting an antigen-specific MHC class I restricted cytotoxic T lymphocyte response and an antigen-specific MHC class II-restricted Th1, Th2 response in an animal, comprising administering (I) to the animal; and

(12) conferring to an animal protective immunity against cancer, comprising administering (I) to the animal.

ACTIVITY - Cytostatic; Antiviral; Antibacterial; Antiparasitic.

The therapeutic effect of empty archaeosomes, and of archaeosomes containing encapsulated **antigen**, on **tumor** growth was evaluated as follows. C57BL/6 mice were first injected with 10X106 EG.7 tumor cells, followed by immunization on days 0 and 10 with nothing (naive), or 15 micro g OVA, or 15 micro g OVA encapsulated in 144 micro g of either T. acidophilum or M. smithii archaeosomes, or with 144 micro g of either type of empty archaeosomes. Injections of OVA alone had no influence on tumor growth/progression. Injecting empty archaeosomes of T. acidophilum resulted in complete regression lof tumors in 2 of 5 mice, and showed similar complete tumor regression and prevented formation of large tumors in the remainder when OVA antigen was encapsulated in the respective archaeosome. Empty archaeosomes of M. smithii had an especially strong therapeutic effect, regressing tumors in 5 of 5 mice.

MECHANISM OF ACTION - **Vaccine**.

USE - The **vaccine** of the invention is useful for conferring protective immunity against an intracellular pathogen, e.g. a virus, bacteria, or a parasite, or against cancer (claimed). Examples of such pathogens include HIV, bacteria that cause tuberculosis, and parasites

that cause malaria.
ADVANTAGE - The **vaccine** of the invention provides an enhance cytotoxic T lymphocyte response.
Dwg.0/25

TECH UPTX: 20010528
TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred **Vaccine**: The pathogen is preferably Francisella tularensis.
Preferred Method: The elicited antigen-specific cytotoxic T cell response is CD8+ T cell mediated. The antigen-specific cytotoxic T cell response in the animal is elicited in the absence of CD4+ T cell help. CD8+ T cell memory response is elicited in the animal. The re-exposure of the animal to the antigen upregulates expression of CD44 memory marker on T cells. The archaeobacterium is selected from Methanobrevibacter smithii, Thermoplasma acidophilum, Halobacterium salinarum, Natronobacterium magadii and Methanosphaera stadtmanae. The polar lipid is isolated in a biologically pure form from an archaeobacterium. The polar lipid is selected from the group consisting of archaetidylglycerol and archaetidyl glycerolphosphate-O-methyl. The intracellular pathogen is selected from virus, a bacterium, a parasite. The antigen is an alkylated peptide amino acid sequence corresponding to an amino acid sequence expressed by the pathogen. The antigen is an isolated outer membrane preparation from the pathogen. The protective immunity is observed in the **vaccinated** animal within 24 to 48 hours after an infectious challenge. The antigen is preferably an isolated outer membrane preparation from Francisella tularensis. The conferred memory response confers to the animal protective immunity over a significant portion of the life span of the animal. An antigen-specific CD4+ T cell and an antigen-specific CD8+ T cell memory response may be elicited in the animal. The antigen is expressed on the surface of the cancer cell.

L12 ANSWER 4 OF 8 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 2001-265996 [27] WPIDS
DNC C2001-080516
TI Novel nucleic acids encoding polyepitope polypeptides containing multiple epitopes from one or more proteins, useful for treating tumors and as **vaccines** against pathogenic agents.
DC A96 B04 **D16**
IN CHICZ, R M; HEDLEY, M L; URBAN, R C
PA (ZYCO-N) ZYCOS INC
CYC 94
PI WO 2001019408 A1 20010322 (200127)* EN 64p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2000075891 A 20010417 (200140)
ADT WO 2001019408 A1 WO 2000-US25559 20000918; AU 2000075891 A AU 2000-75891 20000918
FDT AU 2000075891 A Based on WO 200119408
PRAI US 1999-458173 19991209; US 1999-154665 19990916; US 1999-398534 19990916; US 1999-169846 19991209
AB WO 200119408 A UPAB: 20010518

NOVELTY - A nucleic acid molecule (I) encoding a hybrid polypeptide comprising a signal sequence and three segments that are either contiguous or are separated by a spacer amino acid or spacer peptide, and containing a sequence of at least 11 amino acids, is new.

DETAILED DESCRIPTION - A nucleic acid molecule (I) encoding a hybrid polypeptide comprising a signal sequence and three segments that are either contiguous or are separated by a spacer amino acid or spacer peptide, and containing a sequence of at least 11 amino acids, is new.

The first segment (S1) has the amino acid sequence of a first portion of a naturally occurring **tumor antigen** or naturally occurring protein of a pathogenic agent, and comprises two epitopes (E1).

The second segment (S2) has the amino acid sequence of a second portion of a naturally occurring **tumor antigen** or naturally occurring protein of a pathogenic agent, and comprises two epitopes (E2) different from E1, and the third segment (S3) has the amino acid sequence of a third portion of a naturally occurring **tumor** or **antigen** or naturally occurring protein of a pathogenic agent, and comprises two epitopes (E3) different from E1 and E2, provided that either the first, second and third portions are non-contiguous portions of the same naturally occurring protein, and the sum of all three portions constitutes less than 70% of the sequence of the naturally occurring protein, or the first, second and third portions are portions of three different naturally occurring **tumor antigens** or naturally occurring proteins of one or more pathogenic agents.

INDEPENDENT CLAIMS are also included for the following:

(1) a plasmid or viral vector (II) comprising (I);

(2) a hybrid polypeptide (III) encoded by (I);

(3) a **microsphere** (IV) comprising a polymeric matrix or shell and (I);

(4) a **liposome** comprising (I).

ACTIVITY - Immunostimulatory; antiviral.

MECHANISM OF ACTION - **Vaccine.**

Transgenic HLA-A asterisk 0201/H-2Kb mice were sequentially subjected to, an injection of **microsphere**-encapsulated DNA encoding a polyeptiope polypeptide, and an infection with **vaccinia** virus encoding the polyepitope polypeptide. The **IFN- gamma** ELISPOT assay was used to detect and enumerate T cells specific for DNA-encoded cytotoxic T-lymphocytes (CTL) epitopes in fresh, unexpanded spleen cells. Ten week old mice were injected with PEG/DSPE **microspheres** containing 100 mu g of DNA. 26 days after the **microsphere** injection, mice were infected intraperitoneally with 1x107 plaque forming units of **vaccinia** virus encoding the same polyepitope polypeptide. 9 days after the **vaccinia** boost, spleens were harvested, CD3+ T-cells were enriched, and peptide-specific **IFN- gamma** release was detected using murine **IFN - gamma (interferon-gamma)** ELISPOT. HPV-specific **IFN- gamma** responses were reported as the number of spot-forming cells (SFC)/1 multiply 106 input T-enriched splenocytes. The absolute numbers of SFCs specific for HPV16 E648-56 is 124 for p3KDRa HPV1618 treated groups, and 6 for untreated groups.

USE - (I) and (IV) are useful for eliciting an immune response in a mammal (claimed). (I) and (III) are useful as **vaccines** for treating tumors and pathogenic infections. (I) is useful for preventing or

treating HPV-associated diseases, particularly exophytic condyloma, flat condyloma, cervical cancer, respiratory papilloma, conjunctival papilloma, genital-tract HPV infection, cervical dysplasia, high grade ,mous intraepithelial lesions, and anal HPV infection. (I) and (III) are useful for generating or enhancing prophylactic or therapeutic immune response against pathogens, tumors or autoimmune diseases in a population of individuals having diverse MHC allotypes, as positive controls in T cell stimulation assays in vitro, and as tools to understand processing of epitopes within cells.

ADVANTAGE - Presence of a spacer in between two segments of the hybrid polypeptide will have little or no effect on binding to the MHC molecule. The spacer molecule permits delivery of MHC class I or class II-binding epitopes from polypeptides having only a partial sequence of a pathogen or **tumor antigen**. Hence, problems associated with interference of antigen presentation by viral proteins, or deleterious effects seen in overexpression of particular viral proteins or **tumor antigens**, are avoided. The assortment of epitopes within the polyepitope polypeptides increases a likelihood that at least one epitope will be presented by each of a variety of HLA allotypes. This allows for immunization of a population of individuals polymeric at the HLA locus, using a single hybrid polypeptide or a nucleic acid encoding a polypeptide.

Dwg.0/6

TECH UPTX: 20010518

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Polypeptide: At least one of the segments of (III) comprises three or four epitopes. At least three of the epitopes are MHC (Major histocompatibility complex) class I-binding epitopes. (III) further comprises a fourth segment of at least 11 amino acids, which has the amino acid sequence of a fourth portion of a naturally occurring **tumor antigen** or naturally occurring protein of a pathogenic agent, that is different from the S1, and comprises two epitopes different from E1-E3.

At least one of the segments of (III) is less than 15 amino acids in length and has the sequence of a portion of a human papilloma virus (HPV) protein. Each of the naturally occurring proteins is an HPV protein. At least two, preferably three of the segments are contiguous. Alternately, the first and second segments are separated by a spacer peptide or spacer amino acid which is alanine, and the second and third segments are separated by a spacer peptide or spacer amino acid which is alanine.

(III) comprises a first epitope from a HPV protein and a second epitope which does not overlap with the first epitope and which is from the same or a different HPV protein, where the first epitope binds to a first major histocompatibility complex (MHC) class I allotype and the second epitope binds to a second MHC class I allotype different from the first MHC class I allotype. At least one of the portions is from a HPV strain 16 protein or HPV strain 18 protein, preferably HPV E6 protein or HPV E7 protein. The first and second MHC class I allotype is HLA-A1, HLA-A2, HLA-A3, HLA-A11 or HLA-A24. (III) further comprises a third epitope from an HPV protein, where the third epitope binds to a third MHC class I allotype different from the first and second MHC class I allotypes. (III) comprises 10, 40 or 60 MHC class I allotype-binding epitopes from one or more HPV proteins. E1 overlaps with E3. The signal sequence and the first segment are separated by a spacer amino acid or a spacer peptide. Preferably,

(III) comprises 10 MHC class I-binding epitopes from one HPV protein. (III) comprises a first and second group of HLA-binding epitopes from a HPV strain 16 E6 and/or E7, and/or HPV strain 18 E6 and/or E7 protein. Each group of epitopes comprises at least five epitopes, preferably 15 epitopes, each of which binds to one or more of the allotypes. (III) comprises a targeting signal comprising DRalpha leader sequence MAISGVPVLGFFIIAVLMSAQESWA.
The first, second and third portions are portions of one or more **tumor antigens** expressed from a gene selected from Her2/NEU gene, the prostate specific antigen (PSA) gene, melanoma antigen recognized by T cells (MART) gene and melanoma antigen gene (MAGE). Alternatively, the first, second and third portions are portions of one or more naturally occurring proteins of one or more viruses which infect cells e.g., HPV, HIV, herpes simplex virus (HSV), hepatitis B virus (HBV), hepatitis C virus (HCV), or mycobacteria, Helicobacter spp., Chlamydia spp. or a parasitic eukaryote which infect cells.

L12 ANSWER 5 OF 8 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 2001-123319 [13] WPIDS
DNC C2001-035888
TI Immunogenic compositions comprising Flt-3 ligand encoding polynucleotide and one or more antigen, or cytokine encoding polynucleotides, useful for suppressing tumor growth and for treating autoimmune diseases (e.g. rheumatoid arthritis).
DC B04 **D16**
IN HERMANSON, G G
PA (VICA-N) VICAL INC
CYC 21
PI WO 2001009303 A2 20010208 (200113)* EN 149p
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE
W: CA JP US
ADT WO 2001009303 A2 WO 2000-US20679 20000731
PRAI US 1999-146170 19990730
AB WO 200109303 A UPAB: 20010307
NOVELTY - Immunogenic compositions comprising Flt-3 ligand encoding polynucleotide and one or more antigen or cytokine encoding polynucleotides, are new.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are provided for:
(1) a composition (C1) comprising:
(a) 1 ng to 10 mg of a nucleic acid comprising a first polynucleotide (N1) which hybridizes, at 42 deg. C in 50% formamide, 5 x SSC (saline sodium chloride), 50 mM sodium phosphate, 5 x Denhardt's solution, 10% dextran sulfate, and 20 micro g/ml denatured, sheared salmon sperm DNA, followed by washing at 65 deg. C in 0. 1 x SSC and 0. 1 % sodium dodecyl sulfate (SDS) (w/v), to a reference nucleic acid having a 839, 852, 1152, 663, 519, 1080, 537, or 859 (S1-S8, respectively) nucleotide sequence defined in the specification, or their complements, where the first polynucleotide encodes a polypeptide having immunity-enhancing activity when administered to a vertebrate;
(b) 1 ng to 30 mg of a nucleic acid (N2) comprising a second polynucleotide encoding one or more antigens, or one or more cytokines, where the first and second polynucleotides are non-infectious and non-integrating, and are operably associated with control sequences which direct their expression;

(2) a composition (C2) comprising:

(a) 1 ng to 10 mg of a nucleic acid comprising a first polynucleotide (N3) which encodes a first polypeptide which, except for at least one but not more than 20 amino acid substitutions, deletions, or insertions, is identical to a second polypeptide selected from amino acids 28 to 163 of the 231 amino acid sequence (S9), amino acids 27 to 160 of 235 amino acid sequence (S15), or amino acids 27 to 185 of 235 amino acid sequence (S17) (all sequences are defined in the specification), where the first polypeptide has immunity-enhancing activity when administered to a vertebrate;

(b) 1 ng to 30 mg of N2, where the first and second polynucleotides are non-infectious and non-integrating, and are operably associated with control sequences which direct their expression;

(3) a pharmaceutical composition (C3) comprising:

(a) 1 ng to 10 mg of a nucleic acid molecule comprising a first polynucleotide (N4) encoding an amino acid sequence that is at least 90%, preferably 97%, identical to a reference amino acid sequence selected from S9, 189 (S10), 220 (S11), 232 (S12), 172 (S14), S15, 178 (S16), S17 or 185 (S18) amino acid sequence defined in the specification, where % identity is determined using the Bestfit program with default parameters, and the polypeptide has immunity-enhancing activity when administered to a vertebrate;

(b) 1 ng to 30 mg of N2, where the first and second polynucleotides are non-infectious and non-integrating, and are operably associated with control sequences which direct their expression;

(4) a method (M1) for enhancing an immune response in a vertebrate, comprising administering C1, C2 or C3 to a tissue of the vertebrate, where the first and second polynucleotides are expressed in vivo in an amount effective for a polypeptide expressed by the first polynucleotide to enhance the immunogenicity of one or more antigens, or one or more cytokines; and

(5) a method (M2) of suppressing tumor growth in a mammal, comprising administering C1, C2 or C3 to a tissue of a mammal.

ACTIVITY - Antirheumatic; antiarthritic; immunostimulant; antiviral; antibacterial; antifungal; antiparasitic; cytostatic; immunosuppressive; protozoacide; antiinflammatory.

Three groups of mice were used in the study. One group (n=9) was co-injected with VR6200 (a Flt-3 ligand-encoding plasmid) and VR1623 (bicistronic chimeric Id vector) (100 micro g each) on days 0, 14, and 28, and challenged with 500 38C13 tumor cells two weeks following the last injection. Control groups (n=10 each) were co-injected with VR1623 and VR1051 (control plasmid), or VR1605 (generic cloning vector comprising the constant regions of human kappa light chain and gamma 1 heavy chain separated by a CITE (cap independent translational enhancer)) or alone (200 micro g) on days 0, 14, and 28, and challenged with 500 38C13 tumor cells two weeks following the last injection.

The co-injection of a Flt-3 ligand-encoding plasmid (100 micro g of VR6200) with a **tumor**-specific **antigen**-encoding plasmid (100 micro g of VR1623) significantly enhanced protection from tumor challenge. Eight out of nine mice injected with VR1623 and VR6200 survived

the challenge as compared to zero out of ten mice surviving after being immunized with VR1623 and the control plasmid, VR1051. This increased survival was statistically significant p=0.00007. Furthermore, the co-injection of a Flt-3 ligand-encoding plasmid (VR6200) with an idiotype antigen-encoding plasmid (VR1623) resulted in greatly enhanced anti-Id antibody titer relative to mice injected with VR1623 and VR1051, or with VR1623 alone.

MECHANISM OF ACTION - **Vaccine**.

USE - The compositions are useful for suppressing tumor growth in a mammal. The tumor is melanoma, glioma or lymphoma, particularly B-cell lymphoma. The compositions are used in conjunction with additional cancer treatments (claimed).

The immunogenic compositions can also be used for the prophylactic and/or therapeutic treatment of:

(a) bacterial (e.g. Bacillus infections), viral (e.g. hepatitis B and C in humans), parasitic (e.g. malaria) and fungal infections;

(b) autoimmune diseases (e.g. rheumatoid arthritis and osteoarthritis);

(c) cancer (e.g. cancers of stomach, small intestine, liver, etc.); and

(d) Aujeszky's disease in pigs.

Various other examples of these diseases are given in the specification.

Dwg.0/9

TECH UPTX: 20010307

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Composition: N1 encodes a polypeptide comprising 15, preferably 150, contiguous amino acids of the S9, S10, S11, S12, 220 (S13), S14, S15, S16, S17 or S18. All amino acid sequences are defined in the specification. Preferably, N1 encodes:

(a) residues 28-163, 1-163, 28-189 or 1-189 of S9;
(b) residues 28-231 of S8 and 28-232 of S12;
(c) residues 1-231 of S8 and 1-232 of S12;
(d) residues 28-220, or 1-220 of S11;
(e) residues 28-172 or 1-172 of S14;
(f) residues 27-160, 1-160, 1-185, 27-235, 1-235 or 27-185 of S15;
(g) residues 27-178 or 1-178 of S16; or
(h) residues 1-185, 27-185, 27-235 or 1-235 of S17.

Alternatively, N1 encodes 3 amino acid regions comprising amino acid residues 34-41, 107-113 and 142-150 of S15 arranged consecutively.

Alternatively, N1 encodes a polypeptide selected from:

(a) a polypeptide which, except for at least one amino acid substitution at an amino acid position selected from residues 34, 110, 144, or 147 of S15, is identical to amino acids 27 to 160 of S15; and

(b) a polypeptide which, except for at least one amino acid substitution at an amino acid position selected from residues 34, 110, 144 or 147 of S17, is identical to amino acids 27 to 185 of S17;

The amino acid substitution increases the immunity enhancing activity of the polypeptide.

In C2, the second polypeptide comprises:

(a) residues 1-163, 28-189 or 1-189 of S9;
(b) residues 28-231 of S8 and 28-232 of S12;
(c) residues 1-231 of S8 and 1-232 of S12;
(d) residues 28-220, or 1-220 of S11;
(e) residues 28-172 or 1-172 of S14;
(f) residues 1-160, 1-185, 27-235, 1-235 or 27-185 of S15;
(g) residues 27-178 or 1-178 of S16; or

(h) residues 1-185, 27-235 or 1-235 of S17.
The number of amino acid substitutions, deletions, or insertions is not more than 10, preferably 1. The amino acid substitutions, deletions or insertions do not occur in regions identical to amino acids 34 to 41, 107 to 113, and 142 to 150 of S15.
N3 encodes a polypeptide selected from:
(a) a polypeptide having amino acids 27 to 160 of S15, where at least one amino acid substitution occurs at an amino acid position selected from residues 34, 110, 144 or 147; or
(b) a polypeptide having amino acids 27 to 185 of S17, where at least one amino acid substitution occurs at an amino acid position selected from residues 34, 110, 144 or 147.
The amino acid substitution increases the immunity enhancing activity of the polypeptide.
In all compositions, the nucleic acid molecule of (a) is selected from VR6200 (5322 nucleotide sequence defined in the specification) or VR6230 (5310 nucleotide sequence defined in the specification).
In all the compositions, the antigen is a viral antigen, a bacterial antigen, a protozoan parasite antigen, a helminth parasite antigen, a fungal **antigen**, an ectoparasite **antigen**, a **tumor** associated **antigen**, or a self **antigen** associated with autoimmunity. The **tumor**-associated **antigen** comprises a **tumor**-specific immunoglobulin variable region, a GM2 antigen, a Tn antigen, an sTn antigen, a Thompson-Friedenreich antigen (TF), a Globo H antigen, a Le(y) antigen, a MUC (undefined)-1 antigen, a MUC2 antigen, a MUC3 antigen, a MUC4 antigen, a MUC5AC antigen, a MUC5B antigen, a MUC7 antigen, a carcinoembryonic antigen, a beta chain of human chorionic gonadotropin (hCG beta) antigen, a HER2/neu antigen, a PSMA (undefined) antigen, a EGFRvII (epidermal growth factor receptor vIII) antigen, a KSA (undefined) antigen, a prostate specific antigen (PSA), a PSCA (undefined) antigen, a GP (glycoprotein) 100 antigen, a MAGE-1 (undefined) antigen, a MAGE-2 antigen, a TRP 1 (undefined) antigen, a TRP 2 antigen, or a tyrosinase **antigen**.
The **tumor**-associated **antigen** comprises a B-cell lymphoma-specific idiotype determinant. The **tumor** specific **antigen** further comprises an immunoglobulin constant region. The second polynucleotide encoding the **tumor**-associated **antigen** is polycistronic, i.e. it comprises:
(a) a first cistron encoding a protein comprising a light chain variable region of a B-cell lymphoma immunoglobulin having a tumor-specific idiotype determinant, fused to a constant region; and
(b) a second cistron encoding a protein comprising a heavy chain variable region of a B-cell lymphoma immunoglobulin having a tumor-specific idiotype determinant, fused to a constant region.
The constant region is derived from a heterologous species relative to the variable region. The two cistrons are organized in a transcription unit under the control of a single promoter and the second polynucleotide further comprises an internal ribosome entry site positioned between the cistrons. The second polynucleotide is selected from VR1623 (7521 nucleotide sequence defined in the specification) and VR1642 (7528 nucleotide sequence defined in the specification). The first and second polynucleotides are present in a single nucleic acid molecule which encodes a fusion protein comprising a Flt-3 ligand and one or more antigens, or one or more cytokines.

The compositions further comprise a cationic lipid. The cationic lipid comprises a compound selected from DMRIE ((+/-)-N-(2-hydroxyethyl)-N,N-dimethyl-2,3-bis(tetradecyloxy)-1-propanium bromide), GAP-DMORIE ((+/-)-N-(3-aminopropyl)-N,N-dimethyl-2,3-bis(syn-9-tetradeceneyloxyl)-1-propanaminium bromide) (preferred) or GAP-DLRIE ((+/-)-N-(3-aminopropyl)-N,N-dimethyl-2,3-(bis-dodecylozy)-1-propanaminium bromide). The cationic lipid further comprises one or more co-lipids such as DOPE (undefined), DPyPE (undefined) (preferred) or DMPE (3,4-Dimethoxy-phenylethylamine). The cationic lipid:co-lipid molar ratio ranges from 2:1 to 1:2.

The control sequences are selected from a promoter, an enhancer, an operator, a repressor or a transcription termination signal. Preferably, the control sequence is a promoter selected from cytomegalovirus promoter,

a simian virus 40 promoter or a retrovirus promoter. The first and second polynucleotides are DNA or RNA. The first and second polynucleotides comprise one or more regions regulating cell specific or tissue specific gene expression. The region is tumor cell or tumor tissue specific.

The compositions further comprise 1 ng to 10 mg of a nucleic acid molecule

comprising a third polynucleotide encoding a cytokine, or its active fragment, where the third polynucleotide is non-infectious and non-integrating, and is operably associated with control sequences which direct its expression. The cytokine is selected from Granulocyte macrophage colony stimulating factor (GM-CSF), Granulocyte colony stimulating factor (G-CSF), Macrophage colony stimulating factor (M-CSF), colony stimulating factor (CSF), erythropoietin, interleukin (IL)-2, IL-3,

IL-4, IL-5, IL-6, IL-7, IL-8, IL- 10, IL- 12, IL- 15, IL-18, interferon (**IFN**)-alpha, **IFN**-beta, **IFN-gamma**,

IFN-omega, **IFN**-tau, **IFN-gamma**

inducing factor I, tumor growth factor-beta, RANTES (Regulated upon activation normal T-cell expressed and secreted), Macrophage inflammation protein (MIP)-1-alpha, MIP-1-beta, Leishmania elongation initiating factor

(LEIF), stromal cell derived factor 1 (SDF-1), and MCP-3 (undefined).

Preferred Method: in M1, the tissue is selected from muscle, skin, brain, lung, liver, spleen, bone marrow, thymus, heart, lymph, blood, bone, cartilage, pancreas, kidney, gall bladder, stomach, intestine, testis, ovary, uterus rectum, nervous system, eye, gland, tongue or connective tissue. The vertebrate is a mammal, preferably a human. The construct is free from association with transfection-facilitating proteins, viral particles, **liposomes**, cationic lipids, and calcium phosphate precipitating agents.

In M2, the tumor is selected from melanoma, glioma, or lymphoma. The method further comprises one or more additional cancer treatment methods selected from surgery, radiation therapy, chemotherapy, immunotherapy or gene therapy. The composition is administered prior to the commencement of

the one or more additional cancer treatment methods. Alternatively, the composition is administered during the practice of the one or more additional cancer treatment methods. Alternatively, the composition is administered at the end of one or more additional cancer treatment methods.

L12 ANSWER 6 OF 8 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 2000-422869 [36] WPIDS
DNC C2000-127891

TI Stimulating an immune response to a self antigen by combining a mammalian T cell with a self antigen preparation and a CTLA-4 (T cell counter receptor for B7) blocking agent, useful for treating non-immunogenic and poorly immunogenic tumors.
DC B04 C06 **D16**
IN ALLISON, J P; HURWITZ, A A; VANELSAS, A
PA (REGC) UNIV CALIFORNIA
CYC 88
PI WO 2000032231 A1 20000608 (200036)* EN 96p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW
AU 2000021649 A 20000619 (200044)
ADT WO 2000032231 A1 WO 1999-US28739 19991203; AU 2000021649 A AU 2000-21649 19991203
FDT AU 2000021649 A Based on WO 200032231
PRAI US 1998-110761 19981203
AB WO 200032231 A UPAB: 20000801
NOVELTY - A new method for stimulating an immune response to a self antigen comprises combining a mammalian T cell with an effective dose of a self antigen preparation and a CTLA-4 (T cell counter receptor for B7) blocking agent, where the dose is effective to increase the response of the mammalian T cell to the self antigen.

ACTIVITY - Immunostimulatory.

B16-BL6 was originally derived from the spontaneous murine melanoma cell line B16-F0, by in vitro selection for invasive characteristics. Both parental line and its variant express low levels of H-2Kb and Db, and are negative when stained for (major histocompatibility class (MHC) II. **Vaccination** with irradiated B16-BL6 does not protect against subsequent challenge with live B16-BL6 cells, nor does B7.1 expression result in any significant change in tumor growth in vivo (Chen et al., J Exp. Med. 179:523-532 (1994), unpublished results). Consequently, B16-BL6 can be considered to be poorly immunogenic.

In the experiment, mice received subcutaneous implants of unmodified tumor cells and the treatments (irradiated B16 cells alone, irradiated B16 cells with 9H10 (CTLA-4 blocking agent), and 9H10 alone) at days 0, 3 and 6. CTLA-4 blockade by itself (100 micro g 9H10/dose) had no effect, nor did immunization with irradiated B16 cells at a contralateral site.

However, treatment with both showed a small, but significant and reproducible inhibition of tumor growth, although no cures were obtained. This approach was also used in a protective immunization setting.

Mice were immunized with irradiated B16 cells with and without CTLA-4 blockade (100 micro g 9H10/dose) and with and without cytokine-containing gelatin **microspheres** (containing 50 ng **gamma** - **interferon** and 50 ng granulocyte macrophage colony stimulating factor (GM-CSF). The mice were rechallenged with live, unmodified tumor cells two weeks later. Mice immunized with irradiated cells with CTLA-4 blockade showed significantly impaired tumor growth compared to mice receiving irradiated cells alone. The best protective effect was obtained

with cytokine-containing **microspheres** together with CTLA-4 blockade.

Together, these data indicated that CTLA-4 blockade can enhance immunization strategies employing active immunization with modified tumor cells or tumor fragments, and that it can have a synergistic effect with cytokines.

MECHANISM OF ACTION - The CTLA-4 blocking agent increases the response of the T cells to self antigens.

USE - The method is useful for the treatment of non-immunogenic and poorly immunogenic tumors, as well as other medical conditions requiring selective tissue ablation. The treatment can be applied to humans as well as domestic animals.

Dwg.0/19

TECH UPTX: 20000801

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Method: The mammalian T cell is an autoreactive T cell. The self antigen preparation comprises a self **antigen**, a **tumor** cell lysate or a tumor cell **vaccine**. The tumor cell **vaccine** comprises an irradiated tumor cell transduced to express a cytokine such as granulocyte macrophage colony stimulating factor (GM-CSF). The self antigen comprises a purified antigen selected from tyrosinase, trp1, trp2, melanA/MART1 (undefined), gp100, prostate specific antigen (PSA), prostatic acid phosphatase (PAP), prostate specific membrane antigen (PMSA), prostate stem cell antigen (PSCA), prostase and Her2/neu. The CTLA-4 blocking agent and the self antigen preparation are combined with the mammalian T cell simultaneously.

L12 ANSWER 7 OF 8 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 2000-147169 [13] WPIDS
DNC C2000-046027
TI Systemic immune activation using nucleic acid-lipid complexes used to treat or prevent allergic airway diseases.
DC B04 C06 **D16**
IN DOW, S W; ELMSLIE, R E; SCHWARZE, J
PA (NAJE-N) NAT JEWISH MEDICAL & RES CENT
CYC 85
PI WO 9966879 A2 19991229 (200013)* EN 115p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ UG ZW
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG UZ VN YU ZA ZW
AU 9948272 A 20000110 (200025)
ADT WO 9966879 A2 WO 1999-US14015 19990622; AU 9948272 A AU 1999-48272 19990622
FDT AU 9948272 A Based on WO 9966879
PRAI US 1998-104759 19980625
AB WO 9966879 A UPAB: 20000313

NOVELTY - Eliciting an immune response in a mammal using a genetic immunisation strategy is new.

DETAILED DESCRIPTION - A method to elicit a systemic, non-antigen specific immune response in a mammal comprises administering to the mammal a therapeutic composition by a route of administration chosen from intravenous and intraperitoneal, the therapeutic composition comprising:

(a) a **liposome** delivery vehicle, and

(b) an isolated nucleic acid molecule (I) that is not operatively linked to a transcription control sequence.

INDEPENDENT CLAIMS are also included for the following:

(1) a composition as above;

(2) a method to elicit an immunogen-specific immune response and a systemic, non-specific immune response in a mammal comprising administering to the mammal a therapeutic composition by a route of administration chosen from intravenous and intraperitoneal, the therapeutic composition comprising:

(a) a **liposome** delivery vehicle, and

(b) a recombinant nucleic acid molecule (II) comprising an isolated nucleic acid sequence encoding an immunogen, the sequence being operatively linked to a transcription control sequence; or

(c) a recombinant nucleic acid molecule (III) comprising an isolated nucleic acid sequence encoding a cytokine, the sequence being operatively linked to a transcription control sequence.

ACTIVITY - Cytostatic; Immunoprotective; Anti-viral; Antibacterial; Antifungal.

MECHANISM OF ACTION - Genetic Immunisation.

USE - Administration of the therapeutic composition elicits a systemic, anti-viral or anti-tumour immune response in the mammal. The administration of the therapeutic composition results in a reduction in the tumour or elicits a systemic, protective immune response against allergic inflammation (especially by increasing production of **IFN gamma** or increasing natural killer cell activity) in the mammal. The method and compositions can be used for therapy of humans, dogs, cats, mice, rats, sheep, cattle, horses and pigs. The methods are also useful to elicit an immunogen-specific immune response and a systemic, non-specific immune response in a mammal. The immunogen is chosen from **tumour antigens**, infectious disease pathogen **antigens** (eg. HIV, Mycobacterium tuberculosis, herpes, virus, papilloma virus and Candida) and allergens (plant pollens, drugs, foods, venoms, insect excretions, moulds, animal fluids, hair and dander). The therapeutic compositions can be used to treat or prevent cancer, especially primary lung cancer and pulmonary metastic cancer. The compositions are used to treat or prevent allergic airway diseases, allergic rhinitis, allergic conjunctivitis and food allergy.

ADVANTAGE - Alternate, non-systemic routes of administration significantly decrease both the immunostimulatory effect and therapeutic efficacy of the compositions in comparison with administration by the present method. The nucleic acid:lipid complexes of the present method are useful in human treatments because traditional adjuvants can be avoided. This is advantageous as some adjuvants are toxic and others are relatively ineffective.

DESCRIPTION OF DRAWING(S) - CLRC-mediated immunisation with a tumour RNA with and without DNA encoding a cytokine induces strong antitumour activity in vivo.

Dwg.24/29

TECH UPTX: 20000313

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Composition: (I) is a non-coding sequence. It does not comprise a bacterial nucleic acid sequence. The composition further comprises a recombinant nucleic acid

molecule encoding a cytokine, operatively linked to a transcription control sequence. (II) encoding the immunogen and a nucleic acid encoding a cytokine are in the same recombinant nucleic acid molecule and the sequences are operatively linked to at least one transcription control sequence. (II) comprises a cDNA sequence amplified from total RNA isolated from an autologous tumour sample or from a number of allogeneic tumour samples of the same histological tumour type. The cytokine is chosen from hematopoietic growth factors, interleukins, interferons, immunoglobulin superfamily molecules, tumour necrosis factor family molecules and chemokines. The cytokine is especially IL-2, IL-12 or IFNgamma in the first composition. In the second composition the cytokine is chosen from IL-2, IL-7, IL-12, IL-15, IL-18 and IFNgamma. The **liposome** delivery vehicle comprises lipids chosen from multilamellar vesicle lipids (preferred), extruded lipids or cationic **liposomes**. The vehicle comprises pairs of lipids chosen from DOTMA, DOTAP, DOTIM or DDAB and cholesterol. In particular the lipid pair comprises DOTAP and cholesterol.

The composition has a nucleic acid to lipid ration of from about 1:1 to 1:64. The composition further comprises a pharmaceutically acceptable excipient, especially a non-ionic diluent. The excipient is preferably 5% dextrose in water (D5W).

L12 ANSWER 8 OF 8 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1999-255894 [22] WPIDS
DNC C1999-075085
TI **Tumor vaccine** based on **tumor antigens** comprises a **slow-release** system of **gamma-interferon** (**IFN-gamma**.
DC B04 **D16**
IN CROMMELIN, D J; KIRCHEIS, R; VAN SLOOTEN, M; WAGNER, E; CROMMELIN, D J A; STORM, G
PA (BOEH) BOEHRINGER INGELHEIM INT GMBH
CYC 23
PI DE 19746173 A1 19990422 (199922)* 16p
WO 9920301 A1 19990429 (199924) DE
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE
W: CA JP MX US
EP 1023082 A1 20000802 (200038) EN
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
ADT DE 19746173 A1 DE 1997-19746173 19971018; WO 9920301 A1 WO 1998-EP6546 19981015; EP 1023082 A1 EP 1998-954420 19981015, WO 1998-EP6546 19981015
FDT EP 1023082 A1 Based on WO 9920301
PRAI DE 1997-19746173 19971018
AB DE 19746173 A UPAB: 19990609
NOVELTY - A **tumor vaccine** based on **tumor antigens** also comprises a **slow-release** system of **interferon** (**IFN**)- **gamma** at 50 ng - 5 mu g for 0.5-8.0 hours..
USE - Tumor **vaccine**.
ADVANTAGE - The **slow-release** of **IFN-gamma** leads to a better response in the recipient of the **vaccine**.
Dwg.0/4
TECH UPTX: 19990609
TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred materials: The **IFN-**

gamma is at 100 ng - 2 mug and is released for 2-3 days. About 75% of the **IFN-gamma** is released within 0.5 hours to 3 days. The **slow-release** system comprises a **liposome**, a **microsphere** or a **mini-pellet**. The **tumor antigen** source comprises **tumor** cells, especially allogenic tumor cells. The tumor cells are loaded with **tumor antigen**-derived peptides. Alternatively, the **tumor antigen** source comprises **antigen** presenting cells loaded with **tumor antigen**-derived peptides; or **tumor antigens** or their derivatives.

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FILE COVERS 1969 TO DATE.
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FROM JANUARY 1969 TO DATE.

RECORDS LAST ADDED: 22 August 2001 (20010822/ED)

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     FILE 'BIOSIS' ENTERED AT 10:10:02 ON 23 AUG 2001
L1         15700 S TUMOR (4A) ANTIGEN#
L2         45842 S GAMMA (3A) (IFN OR INTERFERON#)
L3            26 S VACCIN
L4         94672 S VACCIN?
L5            75 S L1 AND L2 AND L4
L6         16483 S  (SLOW OR DELAY? OR CONTROLL? OR TIME# ) (3A) RELEAS?
L7         37707 S LIPOSOM? OR MINIPELLET# OR MICROSPHER? OR MINI PELLET# OR
MIC
L8             2 S L7 AND L5
L9             0 S L5 AND L6
L10        14999 S TUMOR AND L2
L11          537 S L4 AND L10
L12           12 S L11 AND L7
L13            0 S L6 AND L11
L14           12 S L8 OR L12
L15         1167 S MIFNGAMMA OR IFNGAMMA
L16            5 S L15 AND L1 AND L4
L17           17 S L14 OR L16

     FILE 'BIOSIS' ENTERED AT 10:14:48 ON 23 AUG 2001

=> d bib ab it 1-17 l17


L17  ANSWER 1 OF 17  BIOSIS  COPYRIGHT 2001 BIOSIS
AN   2001:382652  BIOSIS
DN   PREV200100382652
TI   Functional maturation of dendritic cells by exposure to CD40L transgenic
     tumor cells, fibroblasts or keratinocytes.
AU   Felzmann, Thomas (1); Buchberger, Maria; Lehner, Manfred; Printz, Dieter;
     Kircheis, Ralf; Wagner, Ernst; Gadner, Helmut; Holter, Wolfgang
CS   (1) St. Anna Children's Hospital, Children's Cancer Research Institute,
     Kinderspitalgasse 6, 1090, Vienna: felzmann@ccri.univie.ac.at Austria
SO   Cancer Letters, (July 26, 2001) Vol. 168, No. 2, pp. 145-154. print.
     ISSN: 0304-3835.
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DT Article
LA English
SL English
AB **Tumor antigen** pulsed dendritic cells (DCs) can induce anti-tumor immunity. We studied strategies for the reliable generation of such a tumor **vaccine** by functional maturation of DCs via interaction of CD40 with its ligand (CD40L, CD154). Exposure of immature DCs to CD40L transgenic cells, soluble recombinant human CD40L molecules or lipopolysaccharide induced expression of the co-stimulatory molecules, CD80 and CD86, and supported an allogeneic mixed leukocyte reaction. In contrast, the release of IL-12, an important mediator of anti-**tumor** immunity, and **antigen**-specific expansion and **IFNgamma** secretion of lymphocytes, was strongly triggered only by DCs exposed to CD40L transgenic cells.
IT Major Concepts
Immune System (Chemical Coordination and Homeostasis); Tumor Biology
IT Parts, Structures, & Systems of Organisms
dendritic cell: immune system, maturation; fibroblasts; keratinocyte: integumentary system; leukocyte: blood and lymphatics, immune system, secretion
IT Chemicals & Biochemicals
CD40; CD40 ligand; CD80; CD86; IFN-gamma [interferon-gamma]: secretion;
lipopolysaccharide
IT Miscellaneous Descriptors
allogenic mixed leukocyte reaction; transgenic tumor cells

L17 ANSWER 2 OF 17 BIOSIS COPYRIGHT 2001 BIOSIS
AN 2001:333076 BIOSIS
DN PREV200100333076
TI Development of Th1-mediated CD8+ effector T cells by **vaccination** with epitope peptides encapsulated in pH-sensitive **liposomes**.
AU Chang, Jin-Soo; Choi, Myeong-Jun; Cheong, Hong-Seok; Kim, Kilhyoun (1)
CS (1) Division of Molecular Life Sciences and College of Pharmacy, Ewha Womans University, 11 Daehyun-dong, Seoul, 120-750: khyounk@mm.ewha.ac.kr South Korea
SO Vaccine, (14 June, 2001) Vol. 19, No. 27, pp. 3608-3614. print.
ISSN: 0264-410X.
DT Article
LA English
SL English
AB There have been many studies for **tumor** therapy mediated by cytotoxic T lymphocytes (CTL) that recognize **tumor**-associated **antigen**. It is generally accepted that CTL responses are induced when antigen is delivered into the cytosol. The pH-sensitive **liposomes** as vehicles are well known for their capacity to deliver the antigen into the cytosol. In this work, immunization of mice with CTL epitope peptides from Hantaan nucleocapsid protein (M6) or human papilloma
virus E7 encapsulated in pH-sensitive **liposomes** induced effective antigen-specific CTL responses. The CTL responses induced by M6 peptide encapsulated in pH-sensitive **liposomes** blocked the formation of **tumor** mass from Hantaan NP transfected B16 melanoma cells in C57BL/6 mice and delayed the growth of preinoculated melanoma cells. During the blockade of the **tumor** growth, the CTL response was maintained for at least approximately 6 weeks, and the mice secreted Th1 type cytokines such as IL-2 and **IFN-gamma**. These

results suggested that the pH-sensitive **liposomes** might provide an effective peptide delivery system for CTL-mediated **tumor** therapy.

IT Major Concepts
Immune System (Chemical Coordination and Homeostasis); **Tumor** Biology

IT Parts, Structures, & Systems of Organisms
CD8-positive effector T cells: blood and lymphatics, immune system; cytotoxic T lymphocyte [CTL]: blood and lymphatics, immune system; **liposome**: antigen delivery vehicle, pH-sensitive

IT Chemicals & Biochemicals
IFN-gamma [**interferon-gamma**]: threonine-1 type cytokine; IL-2 [interleukin-2]: threonine-1 type cytokine; M6 peptide: Hantaan nucleocapsid protein; epitope peptides

IT Methods & Equipment
tumor therapy: therapeutic method; **vaccination**: disease prevention method

IT Miscellaneous Descriptors
tumor growth

ORGN Super Taxa
Muridae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia; Papovaviridae: Animal Viruses, Viruses, Microorganisms

ORGN Organism Name
B16 cell line (Muridae): murine melanoma cells; human papilloma virus (Papovaviridae): strain-E7; mouse (Muridae): animal model, strain-C57BL/6

ORGN Organism Superterms
Animal Viruses; Animals; Chordates; Mammals; Microorganisms; Nonhuman Mammals; Nonhuman Vertebrates; Rodents; Vertebrates; Viruses

L17 ANSWER 3 OF 17 BIOSIS COPYRIGHT 2001 BIOSIS
AN 2001:182398 BIOSIS
DN PREV200100182398
TI **Liposomes** as sustained release system for human **interferon-gamma**: Biopharmaceutical aspects.
AU Van Slooten, M. L.; Boerman, O.; Romoren, K.; Kedar, E.; Crommelin, D. J. A.; Storm, G. (1)
CS (1) Department of Pharmaceutics, Faculty of Pharmacy, Utrecht Institute for Pharmaceutical Sciences (UIPS), Utrecht University, 3508 TB, Utrecht: g.storm@pharm.uu.nl Netherlands
SO Biochimica et Biophysica Acta, (26 February, 2001) Vol. 1530, No. 2-3, pp. 134-145. print.
ISSN: 0006-3002.
DT Article
LA English
SL English
AB **Interferon-gamma** (IFNgamma) has proven to be a promising adjuvant in **vaccines** against cancer and infectious diseases. However, due to its rapid biodegradation and clearance, its efficacy is severely reduced. **Liposomal** association might prolong the residence time of IFNgamma, but no efforts have been made to optimize the biopharmaceutical characteristics of **liposomal** IFNgamma for its application in therapy or as **vaccine** immunoadjuvant. In the present study, various **liposomal** formulations of recombinant human IFNgamma (hIFNgamma), differing in lipid

composition, were prepared via the film hydration method and characterized in vitro regarding association efficiency and bioactivity, and in vivo regarding cytokine release kinetics after subcutaneous (s.c.) administration into mice. Human IFNgamma can be formulated in large, multilamellar **liposomes** with high association efficiency (> 80%) and preservation of bioactivity. A critical parameter is the inclusion of negatively charged phospholipids to obtain a high **liposome** association efficiency, which is dominated by electrostatic interactions. The fraction of externally adsorbed protein compared to the total associated protein can be minimized from 74 +- 9% to 8 +- 3% by increasing the ionic strength of the dispersion medium. After injection of free 125I-hIFNgamma, the radiolabel was detectable up to 48 h at the injection site. **Liposomal** encapsulation of 125I-hIFNgamma increased the local area under the curve 4-fold, and the presence of the radiolabeled hIFNgamma at the injection site was prolonged to 7 days. The release kinetics and overall residence time of the cytokine at the s.c. administration site was influenced by depletion of the externally adsorbed IFNgamma, reducing the initial burst release. Increasing the rigidity of the **liposome** bilayer also resulted in a more pronounced reduction of the burst release and a 19-fold increase in the residence time of the protein at the s.c. administration site, compared to the free cytokine. As adjuvanticity of **liposomal** IFNgamma may strongly depend on the release kinetics of cytokines in vivo, the findings in this paper may contribute to a rational design of **liposomal**-cytokine adjuvants in **vaccines** against cancer and infectious diseases.

IT Major Concepts
Biochemistry and Molecular Biophysics; Methods and Techniques; Pharmaceuticals (Pharmacology)

IT Parts, Structures, & Systems of Organisms
peripheral blood mononuclear cell: blood and lymphatics, immune system

IT Chemicals & Biochemicals
recombinant human **interferon-gamma**: biodegradation, biodistribution, clearance, immunologic - drug, in vivo cytokine release, **liposomal** encapsulation, pharmacokinetics, subcutaneous administration; **tumor** necrosis factor-alpha

IT Methods & Equipment
liposome: biopharmaceutical aspects, drug delivery method, lipid composition, sustained release system

ORGN Super Taxa
Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia; Muridae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia

ORGN Organism Name
human (Hominidae); mouse (Muridae): strain-C57Bl/6

ORGN Organism Superterms
Animals; Chordates; Humans; Mammals; Nonhuman Mammals; Nonhuman Vertebrates; Primates; Rodents; Vertebrates

L17 ANSWER 4 OF 17 BIOSIS COPYRIGHT 2001 BIOSIS
AN 2000:512730 BIOSIS
DN PREV200000512730
TI Pre-existent immunity to the HER-2/neu oncogenic protein in patients with HER-2/neu overexpressing breast and ovarian cancer.
AU Disis, Mary L. (1); Knutson, Keith L.; Schiffman, Kathy; Rinn, Kristine;

McNeel, Douglas G.
CS (1) Oncology, University of Washington, Seattle, WA, 98195-6527 USA
SO Breast Cancer Research and Treatment, (August, 2000) Vol. 62, No. 3, pp. 245-252. print.
ISSN: 0167-6806.
DT Article
LA English
SL English
AB Immunomodulatory strategies, such as antibody therapy and cancer **vaccines**, are increasingly being considered as potential adjuvant therapies in patients with advanced stage breast cancer to either treat minimal residual disease or prevent relapse. However, little is known concerning the incidence and magnitude of the pre-existent breast cancer specific immune response in this patient population. Using the HER-2/neu oncogenic protein as a model, a well-defined **tumor antigen** in breast cancer, we questioned whether patients with advanced stage HER-2/neu overexpressing breast and ovarian cancers (III/IV) had evidence of pre-existent immunity to HER-2/neu. Forty-five patients with stage III or IV HER-2/neu overexpressing breast or ovarian cancer were evaluated for HER-2/neu specific T cell and antibody immunity.

Patients enrolled had not received immunosuppressive chemotherapy for at least 30 days (median 5 months, range 1-75 months). All patients were documented to be immune competent prior to entry by DTH testing using a skin test anergy battery. Five of 45 patients (11%) were found to have a significant HER-2/neu specific T cell response as defined by a stimulation index gtoreq 2.0 (range 2.0-7.9). None of eight patients who were HLA-A2 had a detectable **IFNgamma** secreting T-cell precursor frequency to a well-defined HER-2/neu HLA-A2 T cell epitope, p369-377. Three of 45 patients (7%) had detectable HER-2/neu specific IgG antibodies, range 1.2-8.9 mug/ml. These findings suggest that patients with advanced stage HER-2/neu overexpressing breast and ovarian cancer can mount a T cell and/or antibody immune response to their tumor. However, in the case of the HER-2/neu **antigen**, the pre-existent **tumor** specific immune response is found only in a minority of patients.
IT Major Concepts
Biochemistry and Molecular Biophysics; Immune System (Chemical Coordination and Homeostasis); Tumor Biology
IT Parts, Structures, & Systems of Organisms
T cell: blood and lymphatics, immune system, specific immunity
IT Diseases
breast cancer: neoplastic disease, reproductive system disease/female; ovarian cancer: neoplastic disease, reproductive system disease/female
IT Chemicals & Biochemicals
Her-2/neu antigen; Her-2/neu oncogenic protein: overexpression; cancer **vaccine: vaccine**
IT Alternate Indexing
Breast Neoplasms (MeSH); Ovarian Neoplasms (MeSH)
IT Methods & Equipment
antibody therapy: therapeutic method; immunosuppressive chemotherapy: pharmacological method, therapeutic method; skin test anergy battery: assessment method
IT Miscellaneous Descriptors
pre-existent immunity
ORGN Super Taxa
Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia

ORGN Organism Name
human (Hominidae): patient
ORGN Organism Superterms
Animals; Chordates; Humans; Mammals; Primates; Vertebrates

L17 ANSWER 5 OF 17 BIOSIS COPYRIGHT 2001 BIOSIS
AN 2000:396606 BIOSIS
DN PREV200000396606
TI Transfer of **IFNgamma**-depleted CD4+ T cells together with CD8+ T cells leads to rejection of murine kidney sarcoma in mice.
AU Klugewitz, Katja (1); Scheffold, Alexander; Radbruch, Andreas; Hamann, Alf
CS (1) Experimentelle Rheumatologie, Medizinische Klinik, Charite, Deutsches Rheumaforschungszentrum, Monbijoustr. 2, 10117, Berlin Germany
SO International Journal of Cancer, (1 September, 2000) Vol. 87, No. 5, pp. 673-679. print.
ISSN: 0020-7136.
DT Article
LA English
SL English
AB In the murine kidney sarcoma, **vaccination** with the **tumor** -specific large T **antigen** induces protective immunity against the tumor. Immunity is dependent both on CD8+ cytotoxic T cells and on CD4+ T-helper cells. We analyzed whether the cytokine phenotype of induced CD4+ T-effector cells might determine whether or not the tumor is successfully rejected. By intracytoplasmic staining of CD4+ cells, **IFNgamma**-producing (Th1), IL-4-producing (Th2), and IL-10-expressing cells could be identified in **vaccinated** and non-**vaccinated** animals responding to tumor growth. **Vaccinated** mice rejecting the tumor showed an increase in the percentage of IL-4-producing (Th2) cells. In contrast, in non-**vaccinated** mice succumbing to the tumor, the immunosuppressive IL-10-producing cells became more abundant and the frequency of **IFNgamma**-expressing cells dropped at later time points. Yet, dominance by either a Th1 or a Th2 response could not be observed. To further clarify the relevance of these subsets, Th1 cells were enriched by cell sorting according to **IFNgamma** surface expression. Enriched Th1 and depleted cells, mainly consisting of the Th2 phenotype, were transferred together with CD8+ T cells. Surprisingly, immunity could be transferred either with Th1 or Th2 cells, but Th2 cells were slightly more efficient. This suggests that, at least in the effector phase, a Th1 phenotype is not crucial for the rejection. Our findings support the view that the Th1/Th2 dichotomy is not central in T-cell-mediated tumor rejection.
IT Major Concepts
Urinary System (Chemical Coordination and Homeostasis); Tumor Biology
IT Parts, Structures, & Systems of Organisms
CD4-positive T-effector cells: blood and lymphatics, immune system;
CD4-positive T-helper cells: blood and lymphatics, immune system;
CD8-positive cytotoxic T cells: blood and lymphatics, immune system;
kidney: excretory system
IT Diseases
kidney sarcoma: neoplastic disease, urologic disease
IT Chemicals & Biochemicals

interferon-gamma: production; interleukin-10: expression; interleukin-4: production
IT Methods & Equipment
intracytoplasmic staining: analytical method
IT Miscellaneous Descriptors
T-cell mediated tumor rejection
ORGN Super Taxa
Muridae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
mouse (Muridae): BALB/c, female
ORGN Organism Superterms
Animals; Chordates; Mammals; Nonhuman Mammals; Nonhuman Vertebrates; Rodents; Vertebrates

L17 ANSWER 6 OF 17 BIOSIS COPYRIGHT 2001 BIOSIS
AN 2000:296361 BIOSIS
DN PREV200000296361
TI Gene transfer of human interferon gamma complementary DNA into a renal cell carcinoma line enhances MHC-restricted cytotoxic T lymphocyte recognition but suppresses non-MHC-restricted effector cell activity.
AU Schendel, D. J.; Falk, C. S.; Noessner, E.; Maget, B.; Kressenstein, S.; Urlinger, S.; Tampe, R.; Gansbacher, B.
SO Gene Therapy, (June, 2000) Vol. 7, No. 11, pp. 950-959. print.
ISSN: 0969-7128.
DT Article
LA English
SL English
AB Even though renal cell carcinomas (RCC) are thought to be immunogenic, many tumors express variations in surface molecules and intracellular proteins that hinder induction of optimal antitumor responses. Interferon gamma (**IFNgamma**) stimulation can correct some of these deficiencies. Therefore, we introduced the complementary DNA (cDNA) encoding human **IFNgamma** into a well-characterized RCC line that has been selected for development of an allogeneic tumor cell **vaccine** for treatment of patients with metastatic disease. Studies were performed to determine how endogenous **IFNgamma** expression influences tumor cell immunogenicity. **IFNgamma** transductants showed minimal increases in surface expression of MHC class I and adhesion molecules but expression of class II molecules was induced. Proteins of the transporter associated with antigen processing (TAP) and low molecular weight polypeptide (LMP) were constitutively expressed at high levels. The transductants stimulated allospecific cytotoxic T lymphocytes (CTL); however, they were not better than unmodified tumor cells in this capacity. Endogenous **IFNgamma** expression enhanced tumor cell recognition by MHC-restricted, **tumor antigen**-specific CTL but suppressed recognition by non-MHC-restricted cytotoxic cells. Thus, the functional consequences of **IFNgamma** expression varied with respect to the type of effector cell and were not always beneficial for tumor cell recognition.
IT Major Concepts
Molecular Genetics (Biochemistry and Molecular Biophysics); Pharmacology
IT Parts, Structures, & Systems of Organisms
cytotoxic T lymphocyte: blood and lymphatics, immune system;

non-MHC-restricted cytotoxic cell: blood and lymphatics, immune system
IT Chemicals & Biochemicals
MHC class I [major histocompatibility complex class I]; MHC class II [major histocompatibility complex class II]; adhesion molecules; allogeneic **vaccine**: immunostimulant - drug; cDNA [complementary DNA]; interferon-gamma: expression; transporter associated with antigen processing proteins [TAP proteins]; human INF-gamma gene (Hominidae): expression
IT Miscellaneous Descriptors
non-MHC-restricted effector cell activity suppression; tumor cell recognition
ORGN Super Taxa
Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
renal cell carcinoma-26 cell line (Hominidae)
ORGN Organism Superterms
Animals; Chordates; Humans; Mammals; Primates; Vertebrates
RN 148435-06-7 (TAP PROTEINS)

L17 ANSWER 7 OF 17 BIOSIS COPYRIGHT 2001 BIOSIS
AN 2000:235584 BIOSIS
DN PREV200000235584
TI **Interferon-gamma**-containing **liposomes** as adjuvant in cancer **vaccines**.
AU van Slooten, M. L. (1); Crommelin, D.J.A. (1); Storm, G. (1); Kircheis, R.; Wagner, E.
CS (1) Department of Pharmaceutics, Utrecht University, 3508 TB, Utrecht Netherlands
SO Journal of Controlled Release, (Feb. 14, 2000) Vol. 64, No. 1-3, pp. 328-329.
Meeting Info.: Proceedings of the Fifth European Symposium on Controlled Drug Delivery. Noordwijk aan Zee, Netherlands April 01-03, 1998
ISSN: 0168-3659.
DT Conference
LA English
SL English
IT Major Concepts
Immune System (Chemical Coordination and Homeostasis); Pharmacology; **Tumor** Biology
IT Parts, Structures, & Systems of Organisms
NK cell [natural killer cell]: blood and lymphatics, immune system
IT Chemicals & Biochemicals
MHC [major histocompatibility complex]; cancer **vaccine**: **vaccine; interferon gamma**: adjuvant, cytokine, **liposomes**
IT Methods & Equipment
antitumor **vaccination**: immunization method
IT Miscellaneous Descriptors
Meeting Paper
ORGN Super Taxa
Muridae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
mouse (Muridae): strain-C57bl/6
ORGN Organism Superterms
Animals; Chordates; Mammals; Nonhuman Mammals; Nonhuman Vertebrates; Rodents; Vertebrates

L17 ANSWER 8 OF 17 BIOSIS COPYRIGHT 2001 BIOSIS
AN 2000:162399 BIOSIS
DN PREV200000162399
TI **Liposomes** containing **interferon-gamma** as adjuvant in **tumor** cell **vaccines**.
AU van Slooten, M. L. (1); Storm, G.; Zoephel, A.; Kuepcue, Z.; Boerman, O.; Crommelin, D. J. A.; Wagner, E.; Kircheis, R.
CS (1) Department of Pharmaceutics, Faculty of Pharmacy, Utrecht University, Utrecht Netherlands
SO Pharmaceutical Research (New York)., (Jan., 2000) Vol. 17, No. 1, pp. 42-48.
ISSN: 0724-8741.
DT Article
LA English
SL English
AB Purpose: **Liposomal** systems may be useful as a cytokine supplement in **tumor** cell **vaccines** by providing a cytokine reservoir at the antigen presentation site. Here, we examined the effect of **liposome** incorporation of mIFNgamma on its potency as adjuvant in an established **tumor** cell **vaccination** protocol in the murine B16 melanoma model. Adjuvanticity of the mIFNgamma-**liposomes** was compared to that achieved by mIFNgamma-gene transfection of the B16 **tumor** cells. Furthermore, we studied whether **liposomal** incorporation of mIFNgamma indeed increases the residence time of the cytokine at the **vaccination** site. Methods: C57B1/6 mice were immunized with i) irradiated IFNgamma-gene transfected B16 melanoma cells or ii) irradiated wild type B16 cells supplemented with (**liposomal**) mIFNgamma, followed by a challenge with viable B16 cells. The residence time of the (**liposomal**) cytokine at the subcutaneous (s.c.) **vaccination** site was monitored using radiolabeled mIFNgamma and **liposomes**. Results: Immunization with irradiated **tumor** cells admixed with **liposomal** mIFNgamma generated comparable protection against B16 challenge as immunization with mIFNgamma-gene modified **tumor** cells. Irradiated **tumor** cells admixed with soluble mIFNgamma did not generate any protective responses. Radiolabeling studies indicated that free mIFNgamma rapidly cleared from the s.c. injection site. Association of (125I)-mIFNgamma with **liposomes** increased the local residence time substantially: **liposomal** association of mIFNgamma resulted in a prolonged local residence time of the cytokine as reflected by a 4-fold increase of the area under the curve. The amount of released cytokine in the optimal dose range corresponds to the amount released by the gene-transfected cells. Moderate but significant CTL-activity against B16 cells was found for mice immunized with irradiated cells supplemented with mIFNgamma-**liposomes** compared to untreated control animals. Conclusions: Prolonged presence of mIFNgamma at the site of antigen presentation is crucial for the generation of systemic immune responses in the B16 melanoma model. These studies show that **liposomal** encapsulation of cytokines is an attractive strategy for paracrine cytokine delivery in **tumor** **vaccine** development.
IT Major Concepts
Pharmacology; **Tumor** Biology
IT Parts, Structures, & Systems of Organisms

liposomes
IT Chemicals & Biochemicals
cytokines; **interferon-gamma**; **tumor** cell **vaccines**: antineoplastic activity
IT Methods & Equipment
immunization: immunization method; radiolabeling: detection method
IT Miscellaneous Descriptors
antigen presentation; immune response; **liposomal** drug delivery system; **tumor vaccine** development
ORGN Super Taxa
Muridae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
B16 cell line (Muridae): mouse melanoma cells; mouse (Muridae)
ORGN Organism Superterms
Animals; Chordates; Mammals; Nonhuman Mammals; Nonhuman Vertebrates; Rodents; Vertebrates

L17 ANSWER 9 OF 17 BIOSIS COPYRIGHT 2001 BIOSIS
AN 2000:32734 BIOSIS
DN PREV200000032734
TI LPD lipopolyplex initiates a potent cytokine response and inhibits **tumor** growth.
AU Whitmore, M.; Li, S.; Huang, L. (1)
CS (1) Laboratory of Drug Targeting, Department of Pharmacology, University of Pittsburgh School of Medicine, W1351 Biomedical Sciences Tower, Pittsburgh, PA, 15261 USA
SO Gene Therapy, (Nov., 1999) Vol. 6, No. 11, pp. 1867-1875.
ISSN: 0969-7128.
DT Article
LA English
SL English
AB Our laboratory has recently developed a lipopolyplex consisting of DOTAP:cholesterol **liposomes**, protamine sulfate, and plasmid DNA (LPD) that provides improved systemic gene delivery compared with lipoplex following tail vein injection in mice. Because endothelial cells are the primary cells transfected in the lung, it was hypothesized that LPD might be an effective vector for gene therapy of pulmonary metastases. This hypothesis was examined by testing the efficacy of cytokine (IL-12) and **tumor** suppressor (p53) strategies for treatment of an experimental model of pulmonary metastasis in C57BI/6 mice. Surprisingly, all LPD complexes including those containing an 'empty' plasmid provided a potent (> 50% inhibition) and dose-dependent antitumor effect, compared with dextrose-treated controls. In addition, i.v. injections of LPD containing 'empty' plasmid also inhibited **tumor** growth in a subcutaneous model of C3 fibrosarcomma. The antitumor effect correlated well with a strong and rapidproinflammatory cytokine (TNF-alpha, IL-12 and **IFN -gamma**) response. Naked plasmid DNA did not elicit a cytokine response and the response required assembly of DNA into a lipoplex or the LPD lipopolyplex. Except for the heart, elevated levels of cytokine were observed in all organs (lung, liver, kidney and spleen) where LPD is known to have gene transfer activity. Methylation of immune-stimulatory CpG motifs in the plasmid component of LPD inhibited the proinflammatory cytokine response as well as the antitumor effect of LPD in both **tumor** systems. This suggests that i.v. administration of LPD elicits a systemic proinflammatory cytokine response that mediates the

antitumor activity of the lipopolyplex. In addition, the antitumor activity was not observed in SCID mice suggesting a possible role for B or T lymphocytes in the antitumor response initiated by LPD. This represents the first demonstration that an intravenously administered cationic **liposome**-based nonviral vector can promote a systemic, Th1-like innate immune response. The immune adjuvant properties of LPD might prove to be suitable for delivering **tumor**-specific **antigens** in the context of DNA **vaccination**.

IT Major Concepts
Molecular Genetics (Biochemistry and Molecular Biophysics); Respiratory System (Respiration); **Tumor** Biology

IT Parts, Structures, & Systems of Organisms
B lymphocytes: blood and lymphatics, immune system; T lymphocytes: blood and lymphatics, immune system; lung: respiratory system

IT Diseases
cancer: neoplastic disease, pulmonary metastasis

IT Chemicals & Biochemicals
DOTAP-cholesterol **liposomes**; **IFN-gamma** [**interferon-gamma**]; IL-12 [interleukin-12]; IL-2 [interleukin-2]; LPD lipopolyplex: inhibited **tumor** growth, initiated cytokine response; TNF-alpha [**tumor** necrosis factor-alpha]; p53: **tumor** suppressor; plasmid DNA: effective vector; protamine sulfate

IT Alternate Indexing
Neoplasms (MeSH)

IT Methods & Equipment
gene therapy: therapeutic method

IT Miscellaneous Descriptors
systemic gene delivery

ORGN Super Taxa
Muridae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia

ORGN Organism Name
C3 cell line (Muridae): mouse fibrosarcoma cells; C57Bl/6 mouse (Muridae): animal model; SCID mouse [severe combined immunodeficiency mouse] (Muridae); mouse (Muridae): animal model

ORGN Organism Superterms
Animals; Chordates; Mammals; Nonhuman Mammals; Nonhuman Vertebrates; Rodents; Vertebrates

L17 ANSWER 10 OF 17 BIOSIS COPYRIGHT 2001 BIOSIS
AN 1999:337056 BIOSIS
DN PREV199900337056
TI **Liposomes** as cytokine-supplement in **tumor** cell-based **vaccines**.
AU van Slooten, Maaike L. (1); Kircheis, Ralf; Koppenhagen, Frank J.; Wagner, Ernst; Storm, Gert
CS (1) Department of Pharmaceutics, Utrecht University, 3508 TB, Utrecht Netherlands
SO International Journal of Pharmaceutics (Amsterdam), (June 10, 1999) Vol. 183, No. 1, pp. 33-36.
ISSN: 0378-5173.
DT Article
LA English
SL English

AB Subcutaneous **vaccination** of C57bl/6 mice with irradiated B16 melanoma cells supplemented with **liposomal** interleukin-2 (IL2) or murine **interferon-gamma** (mIFNgamma), resulted in systemic protection in 50% of the animals, against a subsequent **tumor** cell challenge in a dose dependent manner. The protective efficacy was comparable to the efficacy of cytokine gene-modified cells as **tumor vaccine**, whereas irradiated B16 cells supplemented with soluble cytokine did not result in protective responses. In vivo evidence was obtained that the beneficial effects mediated by **liposome** incorporation of the cytokine are the result of a depot function of the **liposomal** cytokine supplement at the **vaccination** site. In can be concluded that **liposomal** delivery of cytokines offers an attractive alternative to cytokine-gene transfection of **tumor** cells for therapeutic **vaccination** protocols.

IT Major Concepts
Clinical Immunology (Human Medicine, Medical Sciences); Oncology (Human Medicine, Medical Sciences); Pharmaceuticals (Pharmacology)

IT Chemicals & Biochemicals
liposomal cytokine supplement: antitumor protection activity, pharmacodynamics, immunologic activity, depot function;
liposomal interferon-gamma [**liposomal interferon-gamma**]: antitumor protection activity, pharmacodynamics, immunologic activity;
liposomal IL-2 [**liposomal** interleukin-2]: antitumor protection activity, pharmacodynamics, immunologic activity;
tumor cell-based **vaccines**: immunostimulant - drug

IT Methods & Equipment
drug delivery particulate systems: drug delivery method

IT Miscellaneous Descriptors
vaccine development

ORGN Super Taxa
Muridae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia

ORGN Organism Name
mouse (Muridae): C57bl/6; B16 cell cell line (Muridae): irradiated; B16 cell line (Muridae): irradiated

ORGN Organism Superterms
Animals; Chordates; Mammals; Nonhuman Mammals; Nonhuman Vertebrates; Rodents; Vertebrates

L17 ANSWER 11 OF 17 BIOSIS COPYRIGHT 2001 BIOSIS
AN 1999:25234 BIOSIS
DN PREV199900025234
TI Delivery of MUC1 mucin peptide by poly(d,l-lactic-co-glycolic acid) **microspheres** induces type 1 T helper immune responses.
AU Newman, Kimberley D.; Sosnowski, Deborah L.; Kwon, Glen S.; Samuel, John (1)
CS (1) 3118 Dentistry/Pharmacy Centre, Fac. Pharmacy and Pharmaceutical Sci., Univ. Alberta, Edmonton, AB T6G 2N8 Canada
SO Journal of Pharmaceutical Sciences, (Nov., 1998) Vol. 87, No. 11, pp. 1421-1427.
ISSN: 0022-3549.
DT Article

LA English
AB Synthetic peptides corresponding to the variable tandem repeat domain of the cancer-associated antigen MUC1 mucin are candidates for cancer **vaccines**. In our investigation mice were immunized via subcutaneous injection with poly(d,l-lactic-co-glycolic acid) (PLGA) **microspheres** containing a MUC1 mucin peptide. It was hypothesized that microencapsulation of the MUC1 mucin peptide would prime for antigen-specific Th1 responses while avoiding the need for traditional adjuvants and carrier proteins. Furthermore, an immunomodulator, monophosphoryl lipid A (MPLA), was incorporated into the peptide-loaded PLGA **microspheres** based on its ability to enhance Th1 responses. The results revealed T cell specific immune responses. The cytokine secretion profiles of the T cells consisted of high levels of **interferon-gamma** with undetectable levels of interleukin-4 and interleukin-10. Moreover, incorporation of MPLA in the MUC1 peptide-loaded PLGA **microspheres** resulted in an increase in **interferon-gamma** production. The antibody response was negative for IgM and IgG in the absence of MPLA; however, in the presence of MPLA antibody production was negative for IgM with a minimal IgG response consisting of IgG2a, IgG2b, and IgG3. Based on the antibody and cytokine profiles, it was concluded that MUC1 mucin peptide-loaded PLGA **microspheres** are capable of eliciting specific Th1 responses, which may be enhanced through the use of MPLA.
IT Major Concepts
Immune System (Chemical Coordination and Homeostasis); Pharmacology; **Tumor** Biology
IT Chemicals & Biochemicals
cancer-associated antigen MUC1; immunoglobulin G isotypes; macromolecules: oral delivery methods; MUC1 mucin peptide: delivery
IT Methods & Equipment
poly(racemic-lactic-co-glycolic acid) **microspheres**: drug delivery method
IT Miscellaneous Descriptors
cancer **vaccine** development; type 1 T helper immune responses
ORGN Super Taxa
Muridae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
mouse (Muridae)
ORGN Organism Superterms
Animals; Chordates; Mammals; Nonhuman Mammals; Nonhuman Vertebrates; Rodents; Vertebrates
RN 34346-01-5 (POLY(D,L-LACTIC-CO-GLYCOLIC ACID))

L17 ANSWER 12 OF 17 BIOSIS COPYRIGHT 2001 BIOSIS
AN 1998:483041 BIOSIS
DN PREV199800483041
TI Irradiated tumor cells adenovirally engineered to secrete granulocyte/macrophage-colony-stimulating factor establish antitumor immunity and eliminate pre-existing tumors in syngeneic mice.
AU Nagai, Eishi; Ogawa, Takahiro; Kielian, Tammy; Ikubo, Akashi; Suzuki, Tsuneo (1)
CS (1) Dep. Microbiol. Mol. Genet. Immunol., Univ. Kansas Med. Cent., 3901 Rainbow Blvd., Kansas City, KS 66160-7420 USA
SO Cancer Immunology Immunotherapy, (Oct., 1998) Vol. 47, No. 2, pp. 72-80. ISSN: 0340-7004.
DT Article
LA English

AB The specific aim of this study was to examine the prophylactic as well as the therapeutic efficacies of irradiated mouse CT26 colon cancer cells, infected with recombinant adenoviruses harboring cDNAs specific for granulocyte macrophage-colony-stimulating factor (GM-CSF), interferon (IFN-gamma) and monocyte chemotactic protein1 (MCP-1). Results showed that tumor cells secrete the respective cytokines for several days after infection and subsequent irradiation. **Vaccination** with irradiated GM-CSF-secreting CT26 cells protected 90% of syngeneic mice challenged with live parental cells. On the other hand, **vaccination** with irradiated **IFNgamma** or MCP-1-secreting CT26 cells totally failed to protect mice from tumor development after challenge with parental cells. None of the tumor-free mice initially **vaccinated** with irradiated GM-CSF-producing CT26 cells developed tumor upon repeated challenge with parental cells during the entire observation period. The establishment of specific and long-lasting antitumor immunity following **vaccination** with GM-CSF-producing tumor cells requires the simultaneous presence of GM-CSF and **tumor antigen** at the **vaccine** site. Depletion of CD8+ cells, but not CD4+ cells, blocked the **vaccine** efficacy of GM-CSF-producing tumor cells. Subcutaneous injection of irradiated GM-CSF-producing CT26 cells also effectively prevented the growth of a small load of parental tumor that was implanted 3 days earlier or the development of metastatic foci in the lung from intravenously injected parental cells either 7 days before or 3 days after **vaccination**. Our data thus show that, in these experimental tumor models, subcutaneous injection of irradiated tumor cells adenovirally, transduced with the GM-CSF gene leads not only to prevention of growth of subsequently implanted tumor but also to elimination of pre-existing and metastatic tumors.

IT Major Concepts
Tumor Biology

ORGN Super Taxa
Muridae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia

ORGN Organism Name
BALB/c mouse (Muridae): animal model; CT26 (Muridae): adenovirus engineering, granulocyte-macrophage colony stimulating factor secretion, immunotherapy model system, **vaccine** preparation, in-vivo tumor treatment, irradiation, mouse colon tumor cell line

ORGN Organism Superterms
Animals; Chordates; Mammals; Nonhuman Mammals; Nonhuman Vertebrates; Rodents; Vertebrates

L17 ANSWER 13 OF 17 BIOSIS COPYRIGHT 2001 BIOSIS
AN 1998:457708 BIOSIS
DN PREV199800457708
TI **Liposomal** encapsulation of cytokines to achieve paracrine cytokine delivery in **tumor vaccine** development.
AU van Slooten, Maaike L. (1); Kircheis, Ralf; Wagner, Ernst; Storm, Gert (1)
CS (1) Dep. Pharmaceutics, Utrecht Univ., PO Box 80.082, 3508 TB Utrecht Netherlands
SO Journal of Liposome Research, (Feb., 1998) Vol. 8, No. 1, pp. 118. Meeting Info.: Sixth Liposome Research Days Conference Les Embiez, France May 28-31, 1998
ISSN: 0898-2104.
DT Conference

LA English
IT Major Concepts
Immune System (Chemical Coordination and Homeostasis); Pharmacology; **Tumor** Biology
IT Parts, Structures, & Systems of Organisms
macrophage: activation, blood and lymphatics, immune system; NK cell [natural killer cell]: activation, blood and lymphatics, immune system
IT Chemicals & Biochemicals
cytokine: **liposomal** encapsulation, paracrine delivery; **interferon-gamma; tumor vaccine; IFN gamma [interferon gamma]:**
murine; MHC [major histocompatibility complex]
IT Miscellaneous Descriptors
antigen presentation; Meeting Abstract
ORGN Super Taxa
Muridae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
mouse (Muridae)
ORGN Organism Superterms
Animals; Chordates; Mammals; Nonhuman Mammals; Nonhuman Vertebrates; Rodents; Vertebrates

L17 ANSWER 14 OF 17 BIOSIS COPYRIGHT 2001 BIOSIS
AN 1998:452725 BIOSIS
DN PREV199800452725
TI Immunogenicity and antitumor activity of a **liposomal** MUC1 peptide-based **vaccine.**
AU Samuel, John; Budzynski, Wladyslaw A.; Reddish, Mark A.; Ding, Lei; Zimmermann, Gabrielle L.; Krantz, Mark J.; Koganty, R. Rao; Longenecker, B. Michael (1)
CS (1) Res. Dev., Biomira Inc., 2011-94 St., Edmonton, AB T6N 1H1 Canada
SO International Journal of Cancer, (Jan. 19, 1998) Vol. 75, No. 2, pp. 295-302.
ISSN: 0020-7136.
DT Article
LA English
AB A human MUC1-transfected mouse mammary adenocarcinoma cell line (GZHI) was used to develop both subcutaneous and intravenous **tumor** models. A **vaccine** formulation comprised of a 24 mer (human MUC1) synthetic peptide encapsulated with monophosphoryl lipid A adjuvant (MPLA) in multilamellar **liposomes** was tested for immunogenicity and anti-**tumor** activity. A low dose of the human MUC1 peptide (5 mug) administered in **liposomes** provided excellent protection of mice in both **tumor** challenge models. The protective antitumor activity mediated by the **liposome** formulation correlated with anti-MUC1-specific T-cell proliferation, **gamma-interferon** (**IFN-gamma**) production and IgG2a anti-MUC1 antibodies, suggesting a type I (TI) T-cell response. In contrast, lack of protection in mice immunized with negative control **vaccines** correlated with IgGI anti-MUC1 antibody formation, low or no anti-MUC1 IgG2. and low antigen-specific T-cell proliferation, consistent with a type 2 (T2) T-cell response to the **tumor.**
IT Major Concepts
Immune System (Chemical Coordination and Homeostasis); Pharmacology; **Tumor** Biology

IT Parts, Structures, & Systems of Organisms
T cell: blood and lymphatics, immune system, proliferation
IT Chemicals & Biochemicals
anti-MUC1 antibodies; **gamma-interferon**: production; **liposomal** MUC1 peptide-based **vaccine**: antitumor activity, immunogenicity, immunostimulant - drug, **vaccine**; monophosphoryl lipid A adjuvant: adjuvant; multilamellar **liposomes**; MUC1 gene
IT Miscellaneous Descriptors
type I T-cell response; **vaccine** development
ORGN Super Taxa
Muridae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
GZHI (Muridae): mammary adenocarcinoma cells
ORGN Organism Superterms
Animals; Chordates; Mammals; Nonhuman Mammals; Nonhuman Vertebrates; Rodents; Vertebrates
RN 95991-05-2 (LIPID A)

L17 ANSWER 15 OF 17 BIOSIS COPYRIGHT 2001 BIOSIS
AN 1997:460255 BIOSIS
DN PREV199799759458
TI Immunological adjuvants and their modes of action.
AU Allison, Anthony C.
CS Dawa Corp., Belmont, CA 94002 USA
SO Archivum Immunologiae et Therapiae Experimentalis, (1997) Vol. 45, No. 2-3, pp. 141-147.
ISSN: 0004-069X.
DT General Review
LA English
AB New adjuvant formulations contain a vehicle, which carries antigens to antigen-presenting cells. Examples of vehicles are **liposomes**, immune-stimulating complexes and microfluidized squalene-in-water emulsions. Adjuvant formulations may contain immunomodulators, which augment cytokine production, such as a synthetic muramyl dipeptide analog or monophosphoryl lipid A. In a primary cascade of cytokine production at the site of antigen + adjuvant injection, TNF-alpha promotes the migration of dendritic cells (DC) to lymphoid tissues while GM-CSF accelerates the differentiation of DC into efficient presenters of antigens to T cells. Adjuvants also up-regulate a secondary cascade of cytokines in lymphoid tissues responding to antigenic stimulation: IL-12 augments the production of **IFN-gamma**, which favors the production of antibodies of protective isotypes (IgG2a in the mouse). Thus adjuvants can regulate immune responses qualitatively as well as quantitatively. Adjuvant formulations can also activate complement, generating C3d, which binds CD21 on follicular dendritic cells (FDC) and B cells. FDC targeting favors the generation of B lymphocyte memory, which is important for **vaccination**.
IT Major Concepts
Blood and Lymphatics (Transport and Circulation); Cell Biology; Clinical Immunology (Human Medicine, Medical Sciences); Immune System (Chemical Coordination and Homeostasis); Pharmacology
IT Chemicals & Biochemicals
SQUALENE

IT Miscellaneous Descriptors
CLINICAL IMMUNOLOGY; CYTOKINES; DENDRITIC CELL; FOLLICULAR DENDRITIC CELL; GRANULOCYTE-MACROPHAGE COLONY STIMULATING FACTOR; IMMUNE SYSTEM; IMMUNOLOGICAL ADJUVANTS; INTERLEUKIN-12; MODES OF ACTION; PHARMACOLOGY;
SQUALENE EMULSIONS; **TUMOR** NECROSIS FACTOR-ALPHA
ORGN Super Taxa
Animalia - Unspecified: Animalia; Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
animal (Animalia - Unspecified); human (Hominidae); Animalia (Animalia - Unspecified)
ORGN Organism Superterms
animals; chordates; humans; mammals; primates; vertebrates
RN 111-02-4 (SQUALENE)

L17 ANSWER 16 OF 17 BIOSIS COPYRIGHT 2001 BIOSIS
AN 1997:206673 BIOSIS
DN PREV199799505876
TI Active immunization with **tumor** cells transduced by a novel AAV plasmid-based gene delivery system.
AU Clary, Bryan M. (1); Coveney, Eamonn C.; Blazeri, Dan G. Ii; Philip, Ramila; Philip, Mohan; Morse, Michael; Gilboa, Eli; Lyerly, H. Kim
CS (1) Dep. Surgery, Duke Univ. Med. Cent., Durham, NC 27710 USA
SO Journal of Immunotherapy, (1997) Vol. 20, No. 1, pp. 26-37.
DT Article
LA English
AB Ex vivo genetically engineered cytokine-secreting **tumor** cell **vaccines** have been shown to prevent metastatic disease in animal models of lung and breast cancer. Because of the inefficiency of existing modes of gene delivery in transducing primary human **tumor** cells, it has been difficult to clinically apply this strategy. In this study, **liposome**-mediated delivery of an adeno-associated virus (AAV)-based plasmid containing the sequence for murine **gamma-interferon** (**gamma-IFN**) (pMP6A-mIFN-**gamma**) was used to generate cytokine-secreting murine **tumor** cell **vaccines**. High levels of **gamma-IFN** and elevated class I major histocompatibility complex expression after transfer of pMP6A-mIFN-gamma into the murine lung cancer cell line, D122, was demonstrated. The efficiency of gene transfer was determined by two different methods and was estimated to be 10-15%. Irradiated **gamma-IFN** D122 cells generated by this novel gene delivery system (D122/pMP6A-mIFN-gamma) and also by standard retroviral methods (DIF2) were administered as weekly **vaccinations** by intraperitoneal injection to animals bearing 7-day-old intrafootpad D122 tumors. Hindlimb amputation was performed when footpad diamteres reached 7 mm, and lungs were harvested 28 days later. Animals **vaccinated** with **gamma-IFN**-secreting D122 cells produced by AAV-based plasmids delivery demonstrated a significant delay in footpad **tumor** growth when compared with controls and DIF2 cells. Fifty-seven percent of animals **vaccinated** with D122/pMP6A-mIFN-gamma were free of pulmonary metastases 28 days after amputation, significantly improved from the 0, 7, and 15% observed in animals **vaccinated** with irradiated parental D122 cells, irradiated D122 cells lipofected with an empty-cassette vector (pMP6A), or
DIF2 cells, respectively. These results and the ability to transfer genes

with this delivery system to a broad range of **tumor** types support its use in the generation of cytokine-secreting **tumor** cell **vaccinations** for use in clinical trials.

IT Major Concepts
Endocrine System (Chemical Coordination and Homeostasis); Genetics; Pathology; Pharmacology; Respiratory System (Respiration); **Tumor** Biology

IT Miscellaneous Descriptors
ACTIVE IMMUNIZATION; ADENO-ASSOCIATED VIRUS-BASED PLASMID; ANTINEOPLASTIC-DRUG; AUTOLOGOUS CYTOKINE GENE-TRANSDUCED **TUMOR** CELLS; CANCER; CANCER **VACCINE** DEVELOPMENT; C57BL/6 MOUSE; DIF2 CELL; DNA TRANSFER METHOD; D122 CELL LINE; **GAMMA-INTERFERON**; GENE DELIVERY VEHICLE; GENE THERAPY; IMMUNE SYSTEM; IMMUNOLOGIC-DRUG; IMMUNOSTIMULANT-DRUG; IRRADIATED **GAMMA-IFN** D122 **TUMOR** CELLS; LIPOFECTION; **LIPOSOME** -MEDIATED PLASMID DELIVERY; METASTASIS CONTROL; MOLECULAR GENETICS; MURINE **GAMMA-INTERFERON** SECRETION; MURINE **GAMMA-INTERFERON** SEQUENCE CONTAINING; MURINE LUNG CANCER CELLS; NEOPLASTIC DISEASE; PHARMACOLOGY; PMP6A-MIFN-GAMMA; RETROVIRAL GENE TRANSFER; RETROVIRAL VECTOR TRANSFORMED CELLS; THERAPEUTIC METHOD; **TUMOR** BIOLOGY; **VACCINE**

ORGN Super Taxa
Muridae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia

ORGN Organism Name
Muridae (Muridae)

ORGN Organism Superterms
animals; chordates; mammals; nonhuman vertebrates; nonhuman mammals; rodents; vertebrates

L17 ANSWER 17 OF 17 BIOSIS COPYRIGHT 2001 BIOSIS
AN 1995:39901 BIOSIS
DN PREV199598054201
TI Cytokines as potential **vaccine** adjuvants.
AU Nohria, Anju; Rubin, Robert H. (1)
CS (1) Massachusetts Inst. Technol., Clin. Res. Cent., 40 Ames St., Build. E18-435, Cambridge, MA 02142-1308 USA
SO Biotherapy (Dordrecht), (1994) Vol. 7, No. 3-4, pp. 261-269. ISSN: 0921-299X.
DT General Review
LA English
AB There is a compelling clinical need for adjuvants suitable for human use to enhance the efficacy of **vaccines** in the prevention of life-threatening infection. Candidate populations for such **vaccine** -adjuvant strategies include normal individuals at the two extremes of life, as well as the ever increasing population of immunocompromised individuals. In addition, adjuvants that would increase the efficiency of **vaccination** with such **vaccines** as those directed against hepatitis B and Streptococcus pneumoniae would have an even greater general use. Cytokines, as natural peptides intimately involved in the normal immune response, have great appeal as potential adjuvants. An increasing body of work utilizing recombinant versions of interleukin-1, -2, -3, -6, -12, **gamma-interferon**, **tumor** necrosis factor, and granulocyte-monocyte-colony stimulating factor has shown that cytokines do have **vaccine** adjuvant activity. However, in order to optimize adjuvant effect and minimize systemic toxicity, strategies in which the cytokine is fused to the antigen, or the cytokine is presented within **liposomes** or **microspheres** appear

to be necessary to make this a practical approach suitable for human use. There is much promise in this approach, but there is much work to be accomplished in order to optimize the pharmacokinetics of cytokine administration as well as its side effect profile.

IT Major Concepts
Blood and Lymphatics (Transport and Circulation); Clinical Immunology (Human Medicine, Medical Sciences); Endocrine System (Chemical Coordination and Homeostasis); Immune System (Chemical Coordination and Homeostasis); Infection; Pharmacology

IT Miscellaneous Descriptors
GRANULOCYTE-MACROPHAGE COLONY STIMULATING FACTOR; IMMUNOCOMPROMISED PATIENT; **INTERFERON-GAMMA**; INTERLEUKIN-1; INTERLEUKIN-12; INTERLEUKIN-2; INTERLEUKIN-3; INTERLEUKIN-6; PHARMACEUTICAL ADJUNCT DRUG FORMULATION; PHARMACEUTICAL FORMULATION; **TUMOR** NECROSIS FACTOR

ORGN Super Taxa
Gram-Positive Cocci: Eubacteria, Bacteria; Hepadnaviridae: Viruses; Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia

ORGN Organism Name
gram-positive cocci (Gram-Positive Cocci); hepatitis B virus (Hepadnaviridae); human (Hominidae); Streptococcus pneumoniae (Gram-Positive Cocci)

ORGN Organism Superterms
animals; bacteria; chordates; eubacteria; humans; mammals; microorganisms; primates; vertebrates; viruses

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=> fil medline

FILE 'MEDLINE' ENTERED AT 10:31:08 ON 23 AUG 2001

 FILE LAST UPDATED: 21 AUG 2001 (20010821/UP).  FILE COVERS 1958 TO DATE.

 On April 22, 2001, MEDLINE was reloaded.  See HELP RLOAD for details.

 MEDLINE now contains IN-PROCESS records.  See HELP CONTENT for details.

 MEDLINE is now updated 4 times per week.  A new current-awareness alert
 frequency (EVERYUPDATE) is available.  See HELP UPDATE for more information.

 MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the
 MeSH 2001 vocabulary.  Enter HELP THESAURUS for details.

 The OLDMEDLINE file segment now contains data from 1958 through 1965.
 Enter HELP CONTENT for details.

 Left, right, and simultaneous left and right truncation are available in the
 Basic Index.  See HELP SFIELDS for details.

 THIS FILE CONTAINS CAS REGISTRY NUMBERS FOR EASY AND ACCURATE
 SUBSTANCE IDENTIFICATION.

=> d his


     (FILE 'BIOSIS' ENTERED AT 10:14:48 ON 23 AUG 2001)
               DEL HIS Y

     FILE 'MEDLINE' ENTERED AT 10:18:53 ON 23 AUG 2001
               E INTERFERON/CT
               E INTERFERON GAMMA/CT
               E E3+ALL
               E  E2+ALL
L1           6 S GAMMA INTERFERON AND VACCIN? AND LIPOS?
L2        8755 S TUMOR AND (GAMMA INTERFERON OR IFN (2A) GAMMA)
L3         379 S L2 AND VACCIN?
L4           7 S L3 AND LIPOS?
L5           0 S INTERFERON TYPE I/+NT/CT
L6       24311 S INTERFERON TYPE II+NT/CT
               E CANCER VACCINES/CT
               E E3+ALL
L7        1444 S CANCER VACCINES/CT
L8       76843 S HIS
L9          93 S L7 AND L6
L10      50407 S LIPOS? OR ENCAPSUL? OR MINIPELLET# OR MICROSPHE? OR MINI
PELL
L11          2 S L9 AND L10
               E CONTROLLED RELEASE/CT
L12          0 S TIME RELEASED/CT
               E TIME RELEASED/CT
L13       2465 S CONTROLLED RELEASE
               E SLOW RELEASED/CT
               E DRUG RELEAS/CT
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L14        10878 S (TIME# OR CONTROL# OR DELAY# OR SLOW) (3A) RELEASE?
L15            0 S L14 AND L9
L16           64 S L14 AND L6
                  E DELAYED"-"ACTION PREPARATIONS/CT
                  E E3+ALL
L17        18521 S DELAYED"-"ACTION PREPARATIONS+NT/CT
L18            0 S L17 AND L9
L19            3 S L7 AND L17
L20            9 S L17 AND L6
L21           11 S L11 OR L20
L22           14 S L19 OR L21

     FILE 'MEDLINE' ENTERED AT 10:31:08 ON 23 AUG 2001

=> d que

L6         24311 SEA FILE=MEDLINE ABB=ON  INTERFERON TYPE II+NT/CT
L7          1444 SEA FILE=MEDLINE ABB=ON  CANCER VACCINES/CT
L9            93 SEA FILE=MEDLINE ABB=ON  L7 AND L6
L10        50407 SEA FILE=MEDLINE ABB=ON  LIPOS? OR ENCAPSUL? OR MINIPELLET#
OR
                  MICROSPHE? OR MINI PELLET# OR MICRO SPHER?
L11            2 SEA FILE=MEDLINE ABB=ON  L9 AND L10
L17        18521 SEA FILE=MEDLINE ABB=ON  DELAYED"-"ACTION PREPARATIONS+NT/CT
L19            3 SEA FILE=MEDLINE ABB=ON  L7 AND L17
L20            9 SEA FILE=MEDLINE ABB=ON  L17 AND L6
L21           11 SEA FILE=MEDLINE ABB=ON  L11 OR L20
L22           14 SEA FILE=MEDLINE ABB=ON  L19 OR L21


=> d .med 1-14


L22  ANSWER 1 OF 14     MEDLINE
AN   2001206923     MEDLINE
DN   21134403   PubMed ID: 11239816
TI   Liposomes as sustained release system for human interferon-gamma:
     biopharmaceutical aspects.
AU   Van Slooten M L; Boerman O; Romoren K; Kedar E; Crommelin D J; Storm G
CS   Department of Pharmaceutics, Utrecht Institute for Pharmaceutical
     Sciences, Utrecht University, Netherlands.
SO   BIOCHIMICA ET BIOPHYSICA ACTA, (2001 Feb 26) 1530 (2-3) 134-45.
     Journal code: A0W; 0217513. ISSN: 0006-3002.
CY   Netherlands
DT   Journal; Article; (JOURNAL ARTICLE)
LA   English
FS   Priority Journals
EM   200104
ED   Entered STN: 20010417
     Last Updated on STN: 20010417
     Entered Medline: 20010412
AB   Interferon-gamma (IFNgamma) has proven to be a promising adjuvant in
     vaccines against cancer and infectious diseases. However, due to its
rapid
     biodegradation and clearance, its efficacy is severely reduced. Liposomal
     association might prolong the residence time of IFNgamma, but no efforts
     have been made to optimize the biopharmaceutical characteristics of
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liposomal IFNgamma for its application in therapy or as vaccine immunoadjuvant. In the present study, various liposomal formulations of recombinant human IFNgamma (hIFNgamma), differing in lipid composition, were prepared via the film hydration method and characterized in vitro regarding association efficiency and bioactivity, and in vivo regarding cytokine release kinetics after subcutaneous (s.c.) administration into mice. Human IFNgamma can be formulated in large, multilamellar liposomes with high association efficiency (>80%) and preservation of bioactivity. A critical parameter is the inclusion of negatively charged phospholipids to obtain a high liposome association efficiency, which is dominated by electrostatic interactions. The fraction of externally adsorbed protein compared to the total associated protein can be minimized from 74+/-9% to 8+/-3% by increasing the ionic strength of the dispersion medium. After injection of free (125)I-hIFNgamma, the radiolabel was detectable up to 48 h at the injection site. Liposomal encapsulation of (125)I-hIFNgamma increased the local area under the curve 4-fold, and the presence of the radiolabeled hIFNgamma at the injection site was prolonged to 7 days. The release kinetics and overall residence time of the cytokine at the s.c. administration site was influenced by depletion of the externally adsorbed IFNgamma, reducing the initial burst release. Increasing the rigidity of the liposome bilayer also resulted in a more pronounced reduction of the burst release and a 19-fold increase in the residence time of the protein at the s.c. administration site, compared to the free cytokine. As adjuvanticity of liposomal IFNgamma may strongly depend on the release kinetics of cytokines in vivo, the findings in this paper may contribute to a rational design of liposomal-cytokine adjuvants in vaccines against cancer and infectious diseases.

CT Check Tags: Animal; Female; Human
Adjuvants, Immunologic: CH, chemistry
***Delayed-Action Preparations**
Injections, Subcutaneous
***Interferon Type II: CH, chemistry**
Interferon Type II: PK, pharmacokinetics
Interferon Type II: PD, pharmacology
Iodine Radioisotopes
*Liposomes: CH, chemistry
Mice
Mice, Inbred C57BL
Monocytes: DE, drug effects
Monocytes: ME, metabolism
Phospholipids: CH, chemistry
Recombinant Proteins: CH, chemistry
Surface Properties
Tumor Necrosis Factor: BI, biosynthesis

L22 ANSWER 2 OF 14 MEDLINE
AN 2000514161 MEDLINE
DN 20523265 PubMed ID: 11073113
TI Morphine enhances interleukin-12 and the production of other pro-inflammatory cytokines in mouse peritoneal macrophages.
AU Peng X; Mosser D M; Adler M W; Rogers T J; Meissler J J Jr; Eisenstein T K
CS Department of Microbiology and Immunology, Temple University School of

Medicine, Philadelphia, Pennsylvania 19140, USA.
NC DA06650 (NIDA)
DA11134 (NIDA)
SO JOURNAL OF LEUKOCYTE BIOLOGY, (2000 Nov) 68 (5) 723-8.
Journal code: IWY; 8405628. ISSN: 0741-5400.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200011
ED Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20001116
AB In this study we investigated the capacity of morphine to modulate expression of cytokines in peritoneal macrophages. Mice were implanted subcutaneously with a 75-mg morphine slow-release pellet, and 48 h later resident peritoneal macrophages were harvested. Control groups received placebo pellets, naltrexone pellets, or morphine plus naltrexone pellets. Adherent cells were stimulated with lipopolysaccharide (LPS: 10 microg/mL) plus interferon-gamma (IFN-gamma: 100 units/mL) to induce cytokine production. After 24 h RNA was extracted for analysis of cytokine mRNA levels by reverse transcriptase-polymerase chain reaction, or supernatants were collected after 48 h for determination of cytokine production by enzyme-linked immunosorbent assay (ELISA). Morphine enhanced mRNA expression of interleukin (IL)-12 p40 and tumor necrosis factor alpha (TNF-alpha) compared with controls, whereas IL-10 levels were unchanged by drug treatment. ELISA data showed that both IL-12 p40 and p70 were increased by morphine. The enhancement of IL-12 at both the mRNA and protein levels was antagonized by naltrexone, indicating that the modulation of this cytokine by morphine is via a classic opioid receptor. These results are particularly interesting in light of our previous observation that 48 h after morphine pellet implantation, the peritoneal cavity is colonized with gram-negative and other enteric bacteria. The enhancement of IL-12 by morphine might be related to morphine-induced sepsis.
CT Check Tags: Animal; Female; Support, U.S. Gov't, P.H.S.
Adjuvants, Immunologic: BI, biosynthesis
Adjuvants, Immunologic: GE, genetics
Analgesics, Opioid: AI, antagonists & inhibitors
*Analgesics, Opioid: PD, pharmacology
Delayed-Action Preparations
Inflammation Mediators
Interferon Type II: PD, pharmacology
Interleukin-10: BI, biosynthesis
Interleukin-10: GE, genetics
*Interleukin-12: BI, biosynthesis
Interleukin-12: GE, genetics
Lipopolysaccharides: PD, pharmacology
*Macrophages, Peritoneal: DE, drug effects
Macrophages, Peritoneal: ME, metabolism
Mice
Mice, Inbred C3H
Morphine: AI, antagonists & inhibitors
*Morphine: PD, pharmacology

Naltrexone: PD, pharmacology
Narcotic Antagonists: PD, pharmacology
RNA, Messenger: BI, biosynthesis
RNA, Messenger: GE, genetics
Stimulation, Chemical
Tumor Necrosis Factor: BI, biosynthesis
Tumor Necrosis Factor: GE, genetics

L22 ANSWER 3 OF 14 MEDLINE
AN 2000482215 MEDLINE
DN 20425371 PubMed ID: 10967281
TI Impaired immunogenicity of immunostimulating complexes (iscoms) by administration in slow-release formulations.
AU Johansson M; Ranlund K; Lovgren-Bengtsson K
CS Swedish University of Agricultural Sciences, Department of Veterinary Microbiology, Section of Virology, BMC, Box 585, S-751 23, Uppsala, Sweden.
SO Microbes Infect, (2000 Jul) 2 (9) 1003-10.
Journal code: DJ1; 100883508. ISSN: 1286-4579.
CY France
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200010
ED Entered STN: 20001019
Last Updated on STN: 20001019
Entered Medline: 20001012
AB This study was performed to explore the possible benefits of formulations and administration regimens that allow a protracted release of iscoms from the injection site. Three forms of slow release of immunostimulating complexes (iscoms) were therefore tested; encapsulation in sodium alginate gel, emulsification in Freund's incomplete adjuvant (FIA) or pulsed-release mimicked by weekly administrations. The administration of iscoms in a depot (alginate or FIA) or in pulses resulted in an antibody response of similar magnitude to that of a traditional two-dose scheme. The character of the immune response was on the other hand affected, i.e. the proportion of specific IgG2a and the IFN-gamma production was decreased by a protracted or repeated release of iscoms, either by a depot or by weekly administrations.
CT Check Tags: Animal; Comparative Study; Female; Support, Non-U.S. Gov't
Alginates
Antigens, Viral: IM, immunology
Bone Marrow: IM, immunology
Cytokines: AN, analysis
Delayed-Action Preparations
Freund's Adjuvant
Gels
*ISCOMs: AD, administration & dosage
*ISCOMs: IM, immunology
IgG: AN, analysis
Influenza A Virus, Human: IM, immunology
Interferon Type II: AN, analysis
Mice
Mice, Inbred BALB C

Pulse Therapy, Drug
Specific Pathogen-Free Organisms
Spleen: CY, cytology
Spleen: IM, immunology
Vaccines, Synthetic: IM, immunology

L22 ANSWER 4 OF 14 MEDLINE
AN 2000177089 MEDLINE
DN 20177089 PubMed ID: 10714607
TI **Liposomes** containing interferon-gamma as adjuvant in tumor cell vaccines.
AU van Slooten M L; Storm G; Zoephel A; Kupcu Z; Boerman O; Crommelin D J; Wagner E; Kircheis R
CS Department of Pharmaceutics, Faculty of Pharmacy, Utrecht University, The Netherlands.. m.l.vanslooten@pharm.uu.nl
SO PHARMACEUTICAL RESEARCH, (2000 Jan) 17 (1) 42-8.
Journal code: PHS; 8406521. ISSN: 0724-8741.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200003
ED Entered STN: 20000330
Last Updated on STN: 20000330
Entered Medline: 20000323
AB PURPOSE: **Liposomal** systems may be useful as a cytokine supplement in tumor cell vaccines by providing a cytokine reservoir at the antigen presentation site. Here, we examined the effect of **liposome** incorporation of mIFNgamma on its potency as adjuvant in an established tumor cell vaccination protocol in the murine B16 melanoma model. Adjuvanticity of the mIFNgamma-**liposomes** was compared to that achieved by mIFNgamma-gene transfection of the B16 tumor cells. Furthermore, we studied whether **liposomal** incorporation of mIFNgamma indeed increases the residence time of the cytokine at the vaccination site. METHODS: C57B1/6 mice were immunized with i) irradiated IFNgamma-gene transfected B16 melanoma cells or ii) irradiated wild type B16 cells supplemented with (**liposomal**) mIFNgamma, followed by a challenge with viable B16 cells. The residence time of the (**liposomal**) cytokine at the subcutaneous (s.c.) vaccination site was monitored using radiolabeled mIFNgamma and **liposomes**. RESULTS: Immunization with irradiated tumor cells admixed with **liposomal** mIFNgamma generated comparable protection against B16 challenge as immunization with mIFNgamma-gene modified tumor cells. Irradiated tumor cells admixed with soluble mIFNgamma did not generate any protective responses. Radiolabeling studies indicated that free mIFNgamma rapidly cleared from the s.c. injection site. Association of [125I]-mIFNgamma with **liposomes** increased the local residence time substantially: **liposomal** association of mIFNgamma resulted in a prolonged local residence time of the cytokine as reflected by a 4-fold increase of the area under the curve. The amount of released cytokine in the optimal dose range corresponds to the amount released by the gene-transfected cells. Moderate but significant CTL-activity against B16 cells was found for mice immunized with irradiated cells supplemented with mIFNgamma-**liposomes** compared to untreated control animals. CONCLUSIONS: Prolonged presence of mIFNgamma at the site of antigen

presentation is crucial for the generation of systemic immune responses in
the B16 melanoma model. These studies show that **liposomal encapsulation** of cytokines is an attractive strategy for paracrine cytokine delivery in tumor vaccine development.
CT Check Tags: Animal; Female; Support, Non-U.S. Gov't
*Adjuvants, Immunologic: AD, administration & dosage
Cancer Vaccines: AD, administration & dosage
***Cancer Vaccines: IM, immunology**
Drug Carriers
***Interferon Type II: AD, administration & dosage**
Interferon Type II: GE, genetics
Liposomes
Melanoma, Experimental: TH, therapy
Mice
Mice, Inbred C57BL
T-Lymphocytes, Cytotoxic: IM, immunology
Transfection
Vaccination

L22 ANSWER 5 OF 14 MEDLINE
AN 2000037341 MEDLINE
DN 20037341 PubMed ID: 10570751
TI Cytokine depot formulations as adjuvants for tumor vaccines. I. Liposome-encapsulated IL-2 as a depot formulation.
AU Krup O C; Kroll I; Bose G; Falkenberg F W
CS Abteilung fur Medizinische Mikrobiologie, Medizinische Fakultat, Ruhr-Universitat Bochum, Germany.
SO JOURNAL OF IMMUNOTHERAPY, (1999 Nov) 22 (6) 525-38.
Journal code: CUQ; 9706083.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199912
ED Entered STN: 20000113
Last Updated on STN: 20000113
Entered Medline: 19991202
AB In an attempt to mimic cytokine gene-transfected tumor cells and to develop an alternative approach to cancer immunotherapy, the authors vaccinated mice with mixtures of inactivated tumor cells and cytokine-containing depots. The RenCa mouse renal carcinoma and the B16 mouse melanoma were used as animal tumor models, with interleukin-2 (IL-2)
as a cytokine and liposomes as a depot form. The results obtained show that vaccines consisting of mixtures of irradiated tumor cells and cytokine-containing liposomes can be used as highly effective tumor vaccines. These vaccines are very easy to prepare and, in contrast to vaccines consisting of cytokine gene transfected tumor cells, their composition (cell dosage, cytokine dosage) can be easily varied. Vaccination efficiency depended on (a) on the immunogenicity of the tumor cells: RenCa tumor cells are more immunogenic than B16 melanoma cells; (b)
vaccination frequency: a single vaccination with irradiated tumor cells and 10 micrograms of IL-2 in liposome-encapsulated form was sufficient to induce lasting protective immunity against the RenCa tumor, whereas several (four to six) vaccinations in weekly intervals were needed to

obtain a similar degree of protective immunity to the B16 melanoma; and (c) the dose of the cytokine encapsulated in the admixed liposome depots: immunity to the tumors could be induced only within a narrow cytokine-dose range ("IL-2-dose window"). The results obtained indicate that, because of the easiness of preparation and handling, vaccine formulations consisting of irradiated tumor cells and IL-2 in depot formulations are candidates for tumor vaccines for the treatment of tumor patients.

CT Check Tags: Animal
*Adjuvants, Immunologic
***Cancer Vaccines**
Cancer Vaccines: TU, therapeutic use
Carcinoma, Renal Cell: IM, immunology
Carcinoma, Renal Cell: PC, prevention & control
Carcinoma, Renal Cell: TH, therapy
Delayed-Action Preparations
Immunotherapy, Active
Interleukin-2: AD, administration & dosage
*Interleukin-2: IM, immunology
Interleukin-2: TU, therapeutic use
Kidney Neoplasms: IM, immunology
Kidney Neoplasms: PC, prevention & control
Kidney Neoplasms: TH, therapy
*Liposomes
Melanoma, Experimental: PC, prevention & control
Mice
Mice, Inbred BALB C
Mice, Inbred C57BL
Neoplasm Transplantation
Spleen: CY, cytology
Vaccination

L22 ANSWER 6 OF 14 MEDLINE
AN 1999399201 MEDLINE
DN 99399201 PubMed ID: 10470215
TI Local intratumor immunotherapy of prostate cancer with interleukin-2 reduces tumor growth.
AU Hautmann S H; Huland E; Huland H
CS Department of Urology, University Hospital of Hamburg, Germany.
SO ANTICANCER RESEARCH, (1999 Jul-Aug) 19 (4A) 2661-3.
Journal code: 59L; 8102988. ISSN: 0250-7005.
CY Greece
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199909
ED Entered STN: 19991012
Last Updated on STN: 19991012
Entered Medline: 19990928
AB BACKGROUND: This study was designed to determine the effectiveness and toxicity of local continuous immunotherapy for prostatic cancer. METHODS: 60 juvenile male Copenhagen rats with Dunning adenocarcinoma of the prostate, implanted subcutaneously into both flanks after proven tumor growth, were treated with either human interleukin-2 (IL-2) depot preparations (n = 30) or albumin (placebo) depot preparations (n = 30) implanted directly next to tumor site. IL-2 depots released IL-2 reliably

for more than 24 days. Rat serum was tested during treatment for human IL-2, possibly absorbed from depots, and for rat interferon gamma. RESULTS: IL-2 treatment reduced tumor growth significantly ($p < 0.001$) compared with albumin treated sites or untreated contralateral sites. No toxicity was observed during treatment. That neither human IL-2 nor rat interferon gamma was detected in serum indicates an exclusively local IL-2
effect. CONCLUSIONS: IL-2 depot preparations reduce tumor growth in Dunning adenocarcinoma of the prostate significantly without toxicity.
CT Check Tags: Animal; Human; Male
*Adenocarcinoma: TH, therapy
Drug Implants
*Immunotherapy
Interferon Type II: BL, blood
Interleukin-2: BL, blood
*Interleukin-2: TU, therapeutic use
Interleukin-2: TO, toxicity
Perfusion, Regional
*Prostatic Neoplasms: TH, therapy
Rats

L22 ANSWER 7 OF 14 MEDLINE
AN 1999290859 MEDLINE
DN 99290859 PubMed ID: 10361150
TI **Liposomes** as cytokine-supplement in tumor cell-based vaccines.
AU van Slooten M L; Kircheis R; Koppenhagen F J; Wagner E; Storm G
CS Department of Pharmaceutics, Utrecht University, PO Box 80.082, 3508 TB, Utrecht, The Netherlands.. m.l.vanslooten@pharm.uu.nl
SO INTERNATIONAL JOURNAL OF PHARMACEUTICS, (1999 Jun 10) 183 (1) 33-6.
Journal code: DA4; 7804127. ISSN: 0378-5173.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199907
ED Entered STN: 19990730
Last Updated on STN: 19990730
Entered Medline: 19990722
AB Subcutaneous vaccination of C57bl/6 mice with irradiated B16 melanoma cells supplemented with **liposomal** interleukin-2 (IL2) or murine interferon-gamma (mIFNgamma), resulted in systemic protection in 50% of the animals, against a subsequent tumor cell challenge in a dose dependent
manner. The protective efficacy was comparable to the efficacy of cytokine
gene-modified cells as tumor vaccine, whereas irradiated B16 cells supplemented with soluble cytokine did not result in protective responses.
In vivo evidence was obtained that the beneficial effects mediated by **liposome** incorporation of the cytokine are the result of a depot function of the **liposomal** cytokine supplement at the vaccination site. In can be concluded that **liposomal** delivery of cytokines offers an attractive alternative to cytokine-gene transfection of tumor cells for therapeutic vaccination protocols. Copyright
CT Check Tags: Animal
***Cancer Vaccines: IM, immunology**
***Interferon Type II: AD, administration & dosage**

Interferon Type II: GE, genetics
*Interleukin-2: AD, administration & dosage
Interleukin-2: GE, genetics
***Liposomes: AD, administration & dosage**
*Melanoma, Experimental: IM, immunology
Mice
Mice, Inbred C57BL
Transfection
Vaccination

L22 ANSWER 8 OF 14 MEDLINE
AN 1999111010 MEDLINE
DN 99111010 PubMed ID: 9815761
TI Characterization of a sustained-release delivery system for combined cytokine/peptide vaccination using a poly-N-acetyl glucosamine-based polymer matrix.
AU Cole D J; Gattoni-Celli S; McClay E F; Metcalf J S; Brown J M; Nabavi N; Newton D A 3rd; Woolhiser C B; Wilson M C; Vournakis J N
CS Departments of Surgery, (Division of Hematology/Oncology), University of South Carolina, Charleston, South Carolina.
SO CLINICAL CANCER RESEARCH, (1997 Jun) 3 (6) 867-73.
Journal code: C2H; 9502500. ISSN: 1078-0432.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199902
ED Entered STN: 19990301
Last Updated on STN: 19990301
. Entered Medline: 19990212
AB Identification of tumor-associated antigens (TAAs) and their class I MHC-restricted epitopes now allows for the rational design of peptide-based cancer vaccines. A biocompatible system capable of sustained release of biologically relevant levels of cytokine and TAA peptide could provide a more effective microenvironment for antigen presentation. Our goal was to test a sustained-release cytokine/TAA peptide-based formulation using a highly purified polysaccharide [poly-N-acetyl glucosamine (p-GlcNAc)] polymer. Granulocyte-macrophage colony-stimulating factor (GM-CSF; 100 microgram) and MART-1(27-35) peptide (128 microgram in DMSO) were formulated into p-GlcNAc. Peptide release was assayed in vitro using interleukin 2 production from previously characterized MART-1(27-35)-specific Jurkat T cells (JRT22). GM-CSF release was assayed via ELISA and proliferation of M-07e (GM-CSF-dependent) cells. Local bioavailability of MART-1(27-35) peptide for uptake and presentation by antigen-presenting cells was demonstrated for up to 6 days (>0.5 microgram/ml). More than 1.0 microgram/ml GM-CSF was concomitantly released over the same period. Biocompatibility and local tissue response to p-GlcNAc releasing murine GM-CSF was determined in C57BL/6 mice via s.c. injection using murine GM-CSF (0. 2 microgram/ml) in 200 microliter of a 2.5% polymer gel. Significant lymphocytic and eosinophilic infiltration was observed 2-7 days after injection with polymer containing murine GM-CSF. The results of our studies show that this biocompatible system is capable of a sustained concomitant release of biologically

active peptide and cytokine into the local microenvironment. These findings support further studies to validate a p-GlcNAc delivery system vehicle for a cytokine/TAA peptide-based cancer vaccine.

CT Check Tags: Animal; Human; Support, Non-U.S. Gov't
*Acetylglucosamine
*Antigens, Neoplasm: AD, administration & dosage
Antigens, Neoplasm: ME, metabolism
Biocompatible Materials
***Cancer Vaccines: AD, administration & dosage**
Cytokines: AD, administration & dosage
Cytokines: PK, pharmacokinetics
Delayed-Action Preparations
*Granulocyte-Macrophage Colony-Stimulating Factor: AD, administration & dosage
*Granulocyte-Macrophage Colony-Stimulating Factor: PK, pharmacokinetics
Jurkat Cells
Mice
Mice, Inbred C57BL
*Neoplasm Proteins: AD, administration & dosage
*Neoplasm Proteins: PK, pharmacokinetics
*Peptide Fragments: AD, administration & dosage
Peptide Fragments: PK, pharmacokinetics
Polysaccharides
Recombinant Proteins: AD, administration & dosage
Recombinant Proteins: PK, pharmacokinetics

L22 ANSWER 9 OF 14 MEDLINE
AN 97399609 MEDLINE
DN 97399609 PubMed ID: 9255709
TI Oral delivery and fate of poly(lactic acid) microsphere-encapsulated interferon in rats.
AU Eyles J E; Alpar H O; Conway B R; Keswick M
CS Pharmaceutical Sciences Institute, Aston University, Birmingham, UK.
SO JOURNAL OF PHARMACY AND PHARMACOLOGY, (1997 Jul) 49 (7) 669-74.
Journal code: JNR; 0376363. ISSN: 0022-3573.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199712
ED Entered STN: 19980109
Last Updated on STN: 19980109
Entered Medline: 19971208

AB In the light of previous findings which suggest that particulate material can be absorbed and thence systemically disseminated from the gastrointestinal tract, we have investigated the oral uptake and distribution of soluble and microsphere-encapsulated radiolabelled interferon-gamma. For trace-loaded (0.01% w/w interferon) microspheres, a quite different distribution of radioactivity was observed in-vivo 15 and 240 min after oral administration, in comparison with the control group which received equivalent doses of unencapsulated interferon-gamma. Thyroid gland activity in control animals killed at these times was significantly higher than that detected in those rodents receiving trace amounts of microencapsulated interferon-gamma ($P < or = 0.05$). For poly(L-lactide) particles with higher interferon loadings (0.97% w/w interferon-gamma) the distinction between the two experimental groups was less significant. During incubation in-vitro, the trace-loaded particles

released a significantly lower percentage of interferon-gamma in comparison with 0.97% w/w loaded microspheres (P < or = 1). Bio-distribution data from rats treated orally with trace amounts of unencapsulated and microencapsulated interferon-gamma leads us to the tentative conclusion that microencapsulation of proteins markedly affects oral uptake, and possibly post-absorption pharmacokinetic parameters also.

CT Check Tags: Animal; Comparative Study; In Vitro; Male; Support, Non-U.S. Gov't
Absorption
Administration, Oral
Delayed-Action Preparations
Drug Compounding
*Drug Delivery Systems
Interferon Type II: AD, administration & dosage
***Interferon Type II: PK, pharmacokinetics**
Interferon Type II: PD, pharmacology
Iodine Radioisotopes
Isotope Labeling
Lactic Acid: CH, chemistry
*Lactic Acid: ME, metabolism
Microspheres
Polymers: CH, chemistry
*Polymers: ME, metabolism
Rats
Rats, Wistar
Thyroid Gland: DE, drug effects
Thyroid Gland: PH, physiology
Tissue Distribution

L22 ANSWER 10 OF 14 MEDLINE
AN 97140600 MEDLINE
DN 97140600 PubMed ID: 8987071
TI Drug delivery issues in vaccine development.
AU Powell M F
CS Genentech, Inc., South San Francisco, California 94080, USA.
SO PHARMACEUTICAL RESEARCH, (1996 Dec) 13 (12) 1777-85. Ref: 132
Journal code: PHS; 8406521. ISSN: 0724-8741.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 199706
ED Entered STN: 19970620
Last Updated on STN: 19970620
Entered Medline: 19970610
AB Although significant headway has been made in vaccine development, there are several delivery-related issues that must be overcome to advance tomorrow's candidate vaccines. Some of these are in the areas of: single-shot subunit vaccines, therapeutic vaccines for cancer, the use of cytokines as vaccine adjuvants, DNA-based vaccines, and the development of vaccines that provide sterilizing immunity, as might be required for an affective HIV-1 prophylactic vaccine. The hurdles for vaccine advancement in these areas are briefly described.

CT Check Tags: Animal; Human
AIDS Vaccines: AD, administration & dosage
Cancer Vaccines: AD, administration & dosage
Cytokines: AD, administration & dosage
Delayed-Action Preparations
Drug Carriers: CH, chemistry
*Drug Delivery Systems: MT, methods
Drug Stability
Immunization: MT, methods
*Vaccines: AD, administration & dosage
Vaccines, DNA: AD, administration & dosage
Vaccines, Synthetic: AD, administration & dosage

L22 ANSWER 11 OF 14 MEDLINE
AN 94084632 MEDLINE
DN 94084632 PubMed ID: 8261390
TI Controlled release, biodegradable cytokine depots: a new approach in cancer vaccine design.
AU Golumbek P T; Azhari R; Jaffee E M; Levitsky H I; Lazenby A; Leong K; Pardoll D M
CS Department of Oncology, School of Medicine, Johns Hopkins University, Baltimore, Maryland 21205.
SO CANCER RESEARCH, (1993 Dec 15) 53 (24) 5841-4.
Journal code: CNF; 2984705R. ISSN: 0008-5472.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199401
ED Entered STN: 19940209
Last Updated on STN: 19970203
Entered Medline: 19940124
AB Experimental studies using murine tumor models have demonstrated that potent systemic immunity can be generated using tumor vaccines engineered by gene transfer to secrete certain cytokines. The underlying physiological principle behind these strategies involves the sustained release of high doses of cytokine at the site of the tumor. In some cases, this paracrine approach appears to enhance tumor antigen presentation and avoids systemic cytokine toxicity. The widespread clinical use of autologous cytokine gene transduced tumor vaccines may be limited by the technical difficulty and labor intensity of individualized gene transfer. We have therefore explored an alternate approach to generating sustained release of cytokines local to the tumor cells. High doses of granulocyte-macrophage colony-stimulating factor encapsulated in cell-sized gelatin-chondroitin sulfate microspheres were mixed with irradiated tumor cells prior to s.c. injection. This vaccination scheme resulted in systemic anti-tumor immune responses comparable to granulocyte-macrophage colony-stimulating factor gene transduced tumor vaccines.
CT Check Tags: Animal; Female; Support, Non-U.S. Gov't
Biodegradation
Delayed-Action Preparations
*Granulocyte-Macrophage Colony-Stimulating Factor: AD, administration & dosage
Granulocyte-Macrophage Colony-Stimulating Factor: TU, therapeutic use
*Immunotherapy, Active

Interferon Type II: AD, administration & dosage
Interferon Type II: TU, therapeutic use
Melanoma, Experimental: IM, immunology
*Melanoma, Experimental: TH, therapy
Mice
Mice, Inbred C57BL
Microspheres
Tumor Cells, Cultured
Vaccination

L22 ANSWER 12 OF 14 MEDLINE
AN 94055958 MEDLINE
DN 94055958 PubMed ID: 8237606
TI Immunosuppressive effects of morphine on immune responses in mice.
AU Eisenstein T K; Bussiere J L; Rogers T J; Adler M W
CS Department of Microbiology and Immunology, Temple University School of Medicine, Philadelphia, PA 19140.
NC NIDA DA-06650 (NIDA)
NIDA T32-07237 (NIDA)
SO ADVANCES IN EXPERIMENTAL MEDICINE AND BIOLOGY, (1993) 335 41-52.
Journal code: 2LU; 0121103. ISSN: 0065-2598.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199312
ED Entered STN: 19940117
Last Updated on STN: 19960129
Entered Medline: 19931215
AB Implantation of a 75-mg morphine sulfate pellet subcutaneously into mice of different strains and sexes caused profound immunosuppression of their spleen cell primary in vitro antibody responses to sheep red blood cells. No sex differences were observed. In mice of the C3H lineage, naltrexone blocked the immunosuppression. In mice in the C57BL/6J lineage, naltrexone was ineffective in blocking the effects of morphine and was itself suppressive. In beige C57BL/6J bgJ/bgJ mice, placebo pellets were also suppressive. The mechanism of the morphine-induced immunosuppression was investigated in C3HeB/FeJ mice. Addition of normal splenic macrophages to in vitro cultures restored immune responses, as did IL-1, IL-6 and IFN-gamma, suggesting that morphine-induced immunosuppression is due to a deficit in macrophage function. Morphine pellet implantation induced splenic atrophy. Whether suppression is attributable to decreased macrophage numbers or to decreased functional capacity of individual macrophages is currently under investigation.
CT Check Tags: Animal; Support, U.S. Gov't, P.H.S.
Antibody Formation: DE, drug effects
Atrophy
Drug Implants
Immune Tolerance
*Immunity: DE, drug effects
Interferon Type II: PD, pharmacology
Interleukin-1: PD, pharmacology
Interleukin-6: PD, pharmacology
Mice
Mice, Inbred C3H
Mice, Inbred C57BL

Morphine: AD, administration & dosage
*Morphine: PD, pharmacology
Spleen: DE, drug effects
Spleen: PA, pathology

L22 ANSWER 13 OF 14 MEDLINE
AN 90358589 MEDLINE
DN 90358589 PubMed ID: 2167647
TI Chemoembolization combined with hepatic arterial induction of endogenous TNF and anticancer agents for hepatocellular carcinoma--a case report.
AU Takekoshi H
CS Dept. of Internal Medicine, Tokyoto Saiseikai Central Hospital.
SO GAN TO KAGAKU RYOHO [JAPANESE JOURNAL OF CANCER AND CHEMOTHERAPY], (1990 Aug) 17 (8 Pt 2) 1744-7.
Journal code: 6T8; 7810034. ISSN: 0385-0684.
CY Japan
DT Journal; Article; (JOURNAL ARTICLE)
LA Japanese
FS Priority Journals
EM 199009
ED Entered STN: 19901026
Last Updated on STN: 19901026
Entered Medline: 19900926
AB Antitumor effect of TNF has been demonstrated to be increased with some kinds of anticancer agents. We reported antitumor effect of hepatic endogenous TNF induced with gamma-IFN and OK-432 for hepatocellular carcinoma (HCC). To increase antitumor effect of transcatheter arterial embolization (TAE), hepatic arterial chemoembolization was performed with a mixture of gamma-IFN, OK-432 and gelatin sponge following a mixture of Doxorubicin and iodized oil (LPO) on the first time. Serum alpha-fetoprotein decreased from 18,903 ng/ml to 470 ng/ml but elevated three months after these procedures. Following the above procedure, hepatic arterial embolization with a mixture of gelatin sponge and Actinomycin D as an inhibitor of RNA was given the second time. Serum alpha-fetoprotein decreased under 5 ng/ml and computed tomography revealed
decreased tumor size and low density area following this second procedure.
Hepatic arterial chemoembolization with a mixture of hepatic induction of endogenous TNF and anticancer agents may well be beneficial for survival of patient with HCC.
CT Check Tags: Case Report; Human; Male
Aged
*Antineoplastic Agents, Combined: AD, administration & dosage
*Biological Products: AD, administration & dosage
*Carcinoma, Hepatocellular: TH, therapy
Dactinomycin: AD, administration & dosage
Delayed-Action Preparations
Doxorubicin: AD, administration & dosage
Drug Administration Schedule
*Embolization, Therapeutic
Gelatin Sponge, Absorbable: AD, administration & dosage
Hepatic Artery
Infusions, Intra-Arterial
***Interferon Type II: AD, administration & dosage**
Iodized Oil: AD, administration & dosage
*Liver Neoplasms: TH, therapy

*Picibanil: AD, administration & dosage
*Tumor Necrosis Factor: PH, physiology

L22 ANSWER 14 OF 14 MEDLINE
AN 89169173 MEDLINE
DN 89169173 PubMed ID: 2494015
TI Local pathological responses to slow-release recombinant interleukin-1, interleukin-2 and gamma-interferon in the mouse and their relevance to chronic inflammatory disease.
AU Dunn C J; Hardee M M; Gibbons A J; Staite N D; Richard K A
CS Department of Hypersensitivity Diseases Research, Upjohn Company, Kalamazoo, Michigan 49001.
SO CLINICAL SCIENCE, (1989 Mar) 76 (3) 261-3.
Journal code: DIZ; 7905731. ISSN: 0143-5221.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 198905
ED Entered STN: 19900306
Last Updated on STN: 19900306
Entered Medline: 19890509
AB 1. The present study describes the pathological responses to local administration of recombinant cytokines in subcutaneously implanted slow-release ethylene vinyl acetate (EVA) co-polymer in mice. 2. EVA-recombinant human interleukin-1 beta (10(4) units) implants induced the formation of chronic granulomatous inflammatory tissue between 4 and 7
days after implantation, characterized by predominant macrophage infiltration, neovascularization and fibrosis which persisted up to 21 days after-implantation. EVA-recombinant human interleukin-1 alpha (10(4)-10(5) units) implants induced a qualitatively similar but less intense response. 3. In contrast, recombinant human interleukin-2 (10(2)-10(4) units) implants resulted in early lymphocytic vasculitis (4 days) and the development of a predominantly lymphoid lesion comprised of lymphoblasts and significant mononuclear cell proliferation by 7 days. 4. EVA-recombinant gamma-interferon (10(3)-10(4) units) implants failed to elicit a significant tissue response; with the exception of multinucleate giant cell formation the characteristics of these lesions closely resembled the mild fibrotic responses observed for EVA-bovine serum albumin (0.5-12.5 mg) implants. 5. These observations suggest that continuous endogenous local release of interleukin-1 or interleukin-2 in vivo is sufficient for the development of specific pathological features characterizing chronic immuno-inflammatory diseases.
CT Check Tags: Animal; Female
Chronic Disease
Delayed-Action Preparations
*Inflammation: ET, etiology
Inflammation: PA, pathology
Interferon-gamma, Recombinant: AD, administration & dosage
***Interferon-gamma, Recombinant: PD, pharmacology**
Interleukin-1: AD, administration & dosage
*Interleukin-1: PD, pharmacology
Interleukin-2: AD, administration & dosage
*Interleukin-2: PD, pharmacology
Mice
Mice, Inbred Strains

Recombinant Proteins: AD, administration & dosage
Recombinant Proteins: PD, pharmacology

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=> fil embase

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     (FILE 'EMBASE' ENTERED AT 10:32:52 ON 23 AUG 2001)
               DEL HIS Y
L1         30436 S GAMMA INTERFERON/CT
L2          1533 S CANCER VACCINE+NT/CT OR TUMOR CELL VACCINE+NT/CT
L3           120 S L1 AND L2
L4         23986 S LIPOS?
L5             7 S L3 AND L4
L6         13527 S MINIPELLET# OR MICROSPHER? OR MINI PELLET# OR MICRO SPHER?
L7             1 S L3 AND L6
L8             0 S CONTROLLED RELEASE FORMULATIONS+NT/CT
L9          1792 S CONTROLLED RELEASE FORMULATION+NT/CT
L10          155 S DELAYED RELEASE FORMULATION+NT/CT
L11          325 S SLOW RELEASE FORMULATION+NT/CT
L12          380 S SUSTAINED RELEASE FORMULATION+NT/CT
L13         1792 S L9 OR L10 OR L11 OR L12
L14            0 S L9 AND L3
L15            2 S L2 AND L13
L16            0 S L1 AND L13 AND VACCIN?
L17            2 S L1 AND L13
L18           12 S L5 OR L7 OR L15 OR L17

     FILE 'EMBASE' ENTERED AT 10:43:39 ON 23 AUG 2001

=> d bib ab ct 1-12


L18  ANSWER 1 OF 12  EMBASE  COPYRIGHT 2001 ELSEVIER SCI. B.V.
AN   2000307926  EMBASE
TI   Impaired immunogenicity of immunostimulating complexes (iscoms) by
     administration in slow-release formulations.
AU   Johansson M.; Ranlund K.; Lovgren-Bengtsson K.
CS   M. Johansson, Swedish Univ. of Agricultural Sci., Dept. of Veterinary
     Microbiology, Box 585, S-751 23 Uppsala, Sweden
SO   Microbes and Infection, (2000) 2/9 (1003-1010).
     Refs: 24
     ISSN: 1286-4579  CODEN: MCINFS
CY   France
DT   Journal; Article
FS   004     Microbiology
     037     Drug Literature Index
     039     Pharmacy
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LA English
SL English
AB This study was performed to explore the possible benefits of formulations and administration regimens that allow a protracted release of iscoms from the injection site. Three forms of slow release of immunostimulating complexes (iscoms) were therefore tested; encapsulation in sodium alginate gel, emulsification in Freund's incomplete adjuvant (FIA) or pulsed-release mimicked by weekly administrations. The administration of iscoms in a depot (alginate or FIA) or in pulses resulted in an antibody response of similar magnitude to that of a traditional two-dose scheme. The character of the immune response was on the other hand affected, i.e. the proportion of specific IgG2a and the IFN-.gamma. production was decreased by a protracted or repeated release of iscoms, either by a depot or by weekly administrations. (C) 2000 Editions scientifiques et medicales Elsevier SAS.
CT Medical Descriptors:
*Influenza virus
***slow release formulation**
*immunomodulation
gel
emulsion
encapsulation
antibody response
interferon induction
immunoglobulin production
nonhuman
male
female
mouse
animal experiment
article
priority journal
Drug Descriptors:
*ISCOM: DV, drug development
*ISCOM: PR, pharmaceutics
*ISCOM: SC, subcutaneous drug administration
alginic acid
Freund adjuvant
immunoglobulin G2a: EC, endogenous compound
gamma interferon: EC, endogenous compound

L18 ANSWER 2 OF 12 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
AN 2000082173 EMBASE
TI **Liposomes** containing interferon-gamma as adjuvant in tumor cell vaccines.
AU Van Slooten M.L.; Storm G.; Zoephel A.; Kupcu Z.; Boerman O.; Crommelin D.J.A.; Wagner E.; Kircheis R.
CS M.L. Van Slooten, Department of Pharmaceutics, Faculty of Pharmacy, Utrecht University, Utrecht, Netherlands. m.l.vanslooten@pharm.uu.nl
SO Pharmaceutical Research, (2000) 17/1 (42-48).
Refs: 30
ISSN: 0724-8741 CODEN: PHREEB
CY United States

DT Journal; Article
FS 026 Immunology, Serology and Transplantation
030 Pharmacology
037 Drug Literature Index
039 Pharmacy
LA English
SL English
AB Purpose. **Liposomal** systems may be useful as a cytokine supplement in tumor cell vaccines by providing a cytokine reservoir at the antigen presentation site. Here, we examined the effect of **liposome** incorporation of mIFN.gamma. on its potency as adjuvant in an established tumor cell vaccination protocol in the murine B16 melanoma model. Adjuvanticity of the mIFN-.gamma.- **liposomes** was compared to that achieved by mIFN.gamma.-gene transfection of the B16 tumor cells. Furthermore, we studied whether **liposomal** incorporation of mIFN.gamma. indeed increases the residence time of the cytokine at the vaccination site. Methods. C57B1/6 mice were immunized with i) irradiated IFN.gamma.-gene transfected B16 melanoma cells or ii) irradiated wild type B16 cells supplemented with (**liposomal**) mIFN.gamma., followed by a challenge with viable B16 cells. The residence time of the (**liposomal**) cytokine at the subcutaneous (s.c.) vaccination site was monitored using radiolabeled mIFN.gamma. and **liposomes**. Results. Immunization with irradiated tumor cells admixed with **liposomal** mIFN.gamma. generated comparable protection against B16 challenge as immunization with mIFN.gamma.-gene modified tumor cells. Irradiated tumor cells admixed with soluble mIFN.gamma. did not generate any protective responses. Radiolabeling studies indicated that free mIFN.gamma. rapidly cleared from the s.c. injection site. Association of [125I]-mIFN.gamma. with **liposomes** increased the local residence time substantially: **liposomal** association of mIFN.gamma. resulted in a prolonged local residence time of the cytokine as reflected by a 4-fold increase of the area under the curve. The amount of released cytokine in the optimal dose range corresponds to the amount released by the gene-transfected cells. Moderate but significant CTL-activity against B16 cells was found for mice immunized with irradiated cells supplemented with mIFN.gamma.-**liposomes** compared to untreated control animals. Conclusions. Prolonged presence of mIFN.gamma. at the site of antigen presentation is crucial for the generation of systemic immune responses in the B16 melanoma model. These studies show that **liposomal** encapsulation of cytokines is an attractive strategy for paracrine cytokine delivery in tumor vaccine development.
CT Medical Descriptors:
*melanoma
antigen presentation
immune response
drug formulation
encapsulation
drug delivery system
nonhuman
female
mouse
animal experiment
animal cell

article
priority journal
Drug Descriptors:
***gamma interferon: DV, drug development**
***gamma interferon: PR, pharmaceutics**
***gamma interferon: SC, subcutaneous drug administration**
***tumor cell vaccine: DV, drug development**
***tumor cell vaccine: PR, pharmaceutics**
***tumor cell vaccine: SC, subcutaneous drug administration**
***liposome**
immunological adjuvant

L18 ANSWER 3 OF 12 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
AN 1999410612 EMBASE
TI Mechanistic investigation of different cytokine controlled release systems
in generating systemic anti-tumor immunity.
AU De la Cruz C.; Liu S.Q.; Leong K.W.
CS C. De la Cruz, Dept. of Biomedical Engineering, Johns Hopkins Univ. School
Medicine, Baltimore, MD 21205, United States
SO Proceedings of the Controlled Release Society, (1999) -/26 (1066-1067).
Refs: 4
ISSN: 1022-0178 CODEN: 58GMAH
CY United States
DT Journal; Article
FS 016 Cancer
026 Immunology, Serology and Transplantation
030 Pharmacology
037 Drug Literature Index
039 Pharmacy
LA English
CT Medical Descriptors:
***controlled release formulation**
*tumor immunity
immunocompetent cell
cell infiltration
lymphocyte
lymph node
drug design
nonhuman
female
mouse
animal experiment
animal model
controlled study
article
Drug Descriptors:
*cytokine: PR, pharmaceutics
microsphere
polymer
granulocyte macrophage colony stimulating factor: PR, pharmaceutics
polyglactin
gelatin
chondroitin sulfate
albumin
heparin

cancer vaccine: DV, drug development
cancer vaccine: PR, pharmaceutics

L18 ANSWER 4 OF 12 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
AN 1999410409 EMBASE
TI Application of protoMASC(TM), a biologically optimised protein PEGylation technology, in cancer vaccination.
AU Wright L.C.; Gardiner A.; Malik F.; Galea-Lauri J.; Delgado C.; Neale D.; Fisher D.; Buckley R.G.; Kippen A.D.; Farzaneh F.; Francis G.E.
CS L.C. Wright, PolyMASC Pharmaceuticals plc, Fleet Road, London NW3 2EZ, United Kingdom
SO Proceedings of the Controlled Release Society, (1999) -/26 (661-662).
Refs: 10
ISSN: 1022-0178 CODEN: 58GMAH
CY United States
DT Journal; Conference Article
FS 027 Biophysics, Bioengineering and Medical Instrumentation
030 Pharmacology
037 Drug Literature Index
039 Pharmacy
LA English
CT Medical Descriptors:
*drug delivery system
vaccination
genetic engineering
controlled release formulation
hydrogel
melanoma
gel permeation chromatography
tumor growth
nonhuman
female
mouse
animal experiment
controlled study
animal cell
conference paper
Drug Descriptors:
***cancer vaccine: DV, drug development**
***cancer vaccine: PR, pharmaceutics**
*macrogol: PR, pharmaceutics
cytokine: PR, pharmaceutics
cytokine: PK, pharmacokinetics
interleukin 2: PR, pharmaceutics

L18 ANSWER 5 OF 12 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
AN 1999306620 EMBASE
TI Immunologic approaches to the treatment of prostate cancer.
AU Harris D.T.; Matyas G.R.; Gomella L.G.; Talor E.; Winship M.D.; Spitler L.E.; Mastrangelo M.J.
CS Dr. D.T. Harris, 100 Lancaster Ave, Wynnewood, PA 19096, United States
SO Seminars in Oncology, (1999) 26/4 (439-447).
Refs: 47
ISSN: 0093-7754 CODEN: SOLGAV
CY United States
DT Journal; Article
FS 016 Cancer

026 Immunology, Serology and Transplantation
037 Drug Literature Index
LA English
SL English
AB The presence of several organ-specific molecules that could serve as immunogens or targets of an immune attack, the nonessential nature of the prostate gland, the substantial failure rate after treatment of the primary tumor, and the lack of effective chemotherapy for metastatic disease make prostate cancer an ideal candidate for immunotherapy. This report reviews the current status of two novel approaches to the treatment of prostate cancer. The first is an effort to induce antitumor immunity by enriching the cytokine environment within the primary cancer by intraprostatic injection of Leukocyte Interleukin (Cei-Sci Corp, Vienna, VA), a mixture of natural cytokines that includes interleukin-1 beta (IL-1.beta.), IL-2, granulocyte- macrophage colony-stimulating factor (GM-CSF), interferon gamma (IFN-.gamma.), and tumor necrosis factor alpha (TNF-.alpha.). The second approach uses Onco Vax-P (Jenner Biotherapies, Inc, San Ramon, CA), a vaccine consisting of **liposome**-encapsulated recombinant prostate-specific antigen (PSA) and lipid A. When administered as an emulsion or in association with bacillus Calmette-Guerin (BCG)/cyclophosphamide or GM-CSF with or without IL-2/cyclophosphamide, immunologic tolerance is broken as evidenced by the generation of humoral and cellular immunity. Both of these approaches have been shown to be feasible and safe, and are now being tested in patients with less advanced disease to determine if manipulation of the immune system can favorably influence clinical outcome.
CT Medical Descriptors:
*prostate cancer: DT, drug therapy
*prostate cancer: PC, prevention
*cancer immunotherapy
tumor immunity
immunological tolerance
humoral immunity
cellular immunity
drug safety
immune system
treatment outcome
immunization
immune response
human
male
female
clinical article
clinical trial
aged
adult
subcutaneous drug administration
intramuscular drug administration
intravenous drug administration
intradermal drug administration
article
priority journal

Drug Descriptors:
*cytokine: CT, clinical trial
*cytokine: DT, drug therapy
*interleukin 1beta: CT, clinical trial
*interleukin 1beta: CB, drug combination
*interleukin 1beta: DT, drug therapy
*recombinant interleukin 2: CT, clinical trial
*recombinant interleukin 2: CB, drug combination
*recombinant interleukin 2: DT, drug therapy
*granulocyte macrophage colony stimulating factor: CT, clinical trial
*granulocyte macrophage colony stimulating factor: CB, drug combination
*granulocyte macrophage colony stimulating factor: DT, drug therapy
***gamma interferon: CT, clinical trial**
***gamma interferon: CB, drug combination**
***gamma interferon: DT, drug therapy**
*tumor necrosis factor alpha: CT, clinical trial
*tumor necrosis factor alpha: CB, drug combination
*tumor necrosis factor alpha: DT, drug therapy
cancer vaccine: CT, clinical trial
cancer vaccine: DT, drug therapy
oncovax p: CT, clinical trial
oncovax p: DT, drug therapy
lipid a: CT, clinical trial
lipid a: CB, drug combination
lipid a: DT, drug therapy
BCG vaccine
cyclophosphamide
prostate specific antigen: CT, clinical trial
prostate specific antigen: CB, drug combination
prostate specific antigen: DT, drug therapy
recombinant granulocyte macrophage colony stimulating factor

L18 ANSWER 6 OF 12 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
AN 1999188323 EMBASE
TI **Liposomes** as cytokine-supplement in tumor cell-based vaccines.
AU Van Slooten M.L.; Kircheis R.; Koppenhagen F.J.; Wagner E.; Storm G.
CS M.L. Van Slooten, Department of Pharmaceutics, Utrecht University, PO Box 80.082, 3508 TB Utrecht, Netherlands. m.l.vanslooten@pharm.uu.nl
SO International Journal of Pharmaceutics, (1999) 183/1 (33-36).
Refs: 17
ISSN: 0378-5173 CODEN: IJPHDE
PUI S 0378-5173(99)00039-3
CY Netherlands
DT Journal; Conference Article
FS 013 Dermatology and Venereology
016 Cancer
026 Immunology, Serology and Transplantation
037 Drug Literature Index
039 Pharmacy
LA English
SL English
AB Subcutaneous vaccination of C57bl/6 mice with irradiated B16 melanoma cells supplemented with **liposomal** interleukin-2 (IL2) or murine interferon-gamma (mIFN.gamma.), resulted in systemic protection in 50% of the animals, against a subsequent tumor cell challenge in a dose dependent manner. The protective efficacy was comparable to the efficacy of cytokine

gene-modified cells as tumor vaccine, whereas irradiated B16 cells supplemented with soluble cytokine did not result in protective responses.

In vivo evidence was obtained that the beneficial effects mediated by **liposome** incorporation of the cytokine are the result of a depot function of the **liposomal** cytokine supplement at the vaccination site. In can be concluded that **liposomal** delivery of cytokines offers an attractive alternative to cytokine-gene transfection of tumor cells for therapeutic vaccination protocols. Copyright (C) 1999 Elsevier Science B.V.

CT Medical Descriptors:
*melanoma b16: PC, prevention
*melanoma b16: DT, drug therapy
irradiation
vaccine production
melanoma cell
genetics
intermethod comparison
nonhuman
mouse
animal model
controlled study
subcutaneous drug administration
conference paper
priority journal
Drug Descriptors:
***tumor cell vaccine: PR, pharmaceutics**
***tumor cell vaccine: DT, drug therapy**
***tumor cell vaccine: DV, drug development**
***tumor cell vaccine: CB, drug combination**
***tumor cell vaccine: AN, drug analysis**
***liposome: CB, drug combination**
*cytokine: PR, pharmaceutics
*cytokine: CB, drug combination
interleukin 2: PK, pharmacokinetics
interleukin 2: CB, drug combination
gamma interferon: PR, pharmaceutics
gamma interferon: CB, drug combination

L18 ANSWER 7 OF 12 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
AN 1998423354 EMBASE
TI Rapid induction of primary human CD4+ and CD8+ T cell responses against cancer-associated MUC1 peptide epitopes.
AU Agrawal B.; Krantz M.J.; Reddish M.A.; Longenecker B.M.
CS B.M. Longenecker, Biomira Inc., 2011-94 Street, Edmonton, Alta. T6N 1H1, Canada
SO International Immunology, (1998) 10/12 (1907-1916).
Refs: 38
ISSN: 0953-8178 CODEN: INIMEN
CY United Kingdom
DT Journal; Article
FS 016 Cancer
026 Immunology, Serology and Transplantation
030 Pharmacology
037 Drug Literature Index
LA English
SL English

AB Antigen-specific MHC class II- and class I-restricted helper and cytotoxic
T cell responses are important anti-cancer immune responses. MUC1 mucin is
a potentially important target for immunotherapy because of its high expression on most human adenocarcinomas. MUC1 peptide-specific type 1 T cell responses were generated in vitro using human peripheral blood lymphocytes (PBL), incubated with **liposomes** containing synthetic MUC1 lipopeptide antigen. Only two weekly stimulations with the **liposomal** MUC1 formulation led to the generation of potent anti-MUC1-specific T cell proliferation as well as class I-restricted cytotoxic responses. Thus the use of PBL pulsed with **liposome** -encapsulated antigen provides an effective approach of rapidly generating
effective antigen-presenting cell (APC) function as well as antigen specific T cells in vitro. It may be feasible to use this technology for the rapid and effective generation of APC and/or T cells as cellular vaccines for adenocarcinomas.

CT Medical Descriptors:
*cytotoxic t lymphocyte
*cancer immunotherapy
t lymphocyte
helper cell
immune response
protein expression
adenocarcinoma: ET, etiology
lymphocyte
cell proliferation
antigen presenting cell
antigen specificity
phenotype
cell culture
cytokine production
enzyme linked immunosorbent assay
t lymphocyte activation
human
controlled study
human cell
article
priority journal
Drug Descriptors:
*cd4 antigen: EC, endogenous compound
*cd8 antigen: EC, endogenous compound
*mucin: EC, endogenous compound
epitope: EC, endogenous compound
major histocompatibility antigen class 2: EC, endogenous compound
liposome
cancer vaccine: DV, drug development
gamma interferon: EC, endogenous compound
interleukin 4: EC, endogenous compound

L18 ANSWER 8 OF 12 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
AN 1998149687 EMBASE
TI Cancer vaccines (Part 2 of 2).
AU Hallin P.A.; Adams V.R.
SO Journal of the American Pharmaceutical Association, (1997) 37/6 (706-709).

Refs: 16
ISSN: 1086-5802 CODEN: JPHAF8
CY United States
DT Journal; (Short Survey)
FS 016 Cancer
026 Immunology, Serology and Transplantation
037 Drug Literature Index
038 Adverse Reactions Titles
039 Pharmacy
LA English
CT Medical Descriptors:
*cancer immunotherapy
*vaccination
melanoma: DT, drug therapy
colorectal cancer: DT, drug therapy
kidney carcinoma: DT, drug therapy
breast cancer: DT, drug therapy
ovary cancer: DT, drug therapy
lung cancer: DT, drug therapy
uterine cervix cancer: DT, drug therapy
pain: SI, side effect
skin manifestation: SI, side effect
fever: SI, side effect
myalgia: SI, side effect
arthralgia: SI, side effect
delayed hypersensitivity
cytotoxic t lymphocyte
humoral immunity
corynebacterium parvum
cancer survival
human
clinical trial
phase 1 clinical trial
phase 2 clinical trial
phase 3 clinical trial
short survey
Drug Descriptors:
***cancer vaccine: AE, adverse drug reaction**
***cancer vaccine: CT, clinical trial**
***cancer vaccine: DT, drug therapy**
***cancer vaccine: PR, pharmaceutics**
*tumor antigen
*vaccinia vaccine: CT, clinical trial
*vaccinia vaccine: DT, drug therapy
*immunological adjuvant
***liposome**
melanoma vaccine: CT, clinical trial
melanoma vaccine: DT, drug therapy
melanoma vaccine: PR, pharmaceutics
bcg vaccine: AE, adverse drug reaction
granulocyte macrophage colony stimulating factor
gamma interferon
interleukin 1
interleukin 2
aluminum potassium sulfate
phosphoryl lipid a
immunoglobulin g: EC, endogenous compound

immunoglobulin m: EC, endogenous compound

L18 ANSWER 9 OF 12 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
AN 1998006551 EMBASE
TI Active immunization with tumor cells transduced by a novel AAV plasmid-based gene delivery system.
AU Clary B.M.; Coveney E.C.; Blazer III D.G.; Philip R.; Philip M.; Morse M.;
Gilboa E.; Lyerly H.K.
CS Dr. B.M. Clary, Department of Surgery, Duke University Medical Center, Durham, NC 27710, United States
SO Journal of Immunotherapy, (1997) 20/1 (26-37).
Refs: 37
ISSN: 1053-8550 CODEN: JOIME7
CY United States
DT Journal; Article
FS 016 Cancer
026 Immunology, Serology and Transplantation
037 Drug Literature Index
LA English
SL English
AB Ex vivo genetically engineered cytokine-secreting tumor cell vaccines have
been shown to prevent metastatic disease in animal models of lung and breast cancer. Because of the inefficiency of existing modes of gene delivery in transducing primary human tumor cells, it has been difficult to clinically apply this strategy. In this study, **liposome**-mediated delivery of an adeno- associated virus (AAV)-based plasmid containing the sequence for murine .gamma.- interferon (.gamma.-IFN) (pMP6A-mIFN-.gamma.) was used to generate cytokine-secreting murine tumor cell vaccines. High levels of .gamma.-IFN and elevated class I major histocompatibility complex expression after transfer of pMP6A-mIFN-.gamma.
into the murine lung cancer cell line, D122, was demonstrated. The efficiency of gene transfer was determined by two different methods and was estimated to be 10-15%. Irradiated .gamma.-IFN D122 cells generated by
this novel gene delivery system (D122/pMP6A-mIFN-.gamma.) and also by standard retroviral methods (DIF2) were administered as weekly vaccinations by intraperitoneal injection to animals bearing 7-day-old intrafootpad D122 tumors. Hindlimb amputation was performed when footpad diameters reached 7 mm, and lungs were harvested 28 days later. Animals vaccinated with .gamma.-IFN-secreting D122 cells produced by AAV-based plasmids delivery demonstrated a significant delay in foot-pad tumor growth when compared with controls and DIF2 cells. Fifty-seven percent of animals vaccinated with D122/pMP6A-mIFN-.gamma. were free of pulmonary metastases 28 days after amputation, significantly improved from the 0, 7,
and 15% observed in animals vaccinated with irradiated parental D122 cells, irradiated D122 cells lipofected with an empty-cassette vector (pMP6A), or DIF2 cells, respectively. These results and the ability to transfer genes with this delivery system to a broad range of tumor types support its use in the generation of cytokine-secreting tumor cell vaccinations for use in clinical trials.
CT Medical Descriptors:
*gene targeting
*active immunization

*cancer immunization
genetic engineering
drug effect
metastasis inhibition
virus vector
adeno associated virus
interferon production
foot pad
cancer inhibition
drug efficacy
nonhuman
male
mouse
animal experiment
animal model
article
priority journal
Drug Descriptors:
***cancer vaccine: PD, pharmacology**
gamma interferon

L18 ANSWER 10 OF 12 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
AN 97098519 EMBASE
DN 1997098519
TI Effect of slow release IL-12 and IL-10 on inflammation, local macrophage function and the regional lymphoid response during mycobacterial (Th1) and schistosomal (Th2) antigen-elicited pulmonary granuloma formation.
AU Chensue S.W.; Warmington K.; Ruth J.H.; Kunkel S.L.
CS S.W. Chensue, Dept. Pathology Laboratory Medicine, Veterans Affairs Medical Center, 2215 Fuller Rd, Ann Arbor, MI 48105, United States
SO Inflammation Research, (1997) 46/3 (86-92).
Refs: 36
ISSN: 1023-3830 CODEN: INREFB
CY Switzerland
DT Journal; Article
FS 015 Chest Diseases, Thoracic Surgery and Tuberculosis
026 Immunology, Serology and Transplantation
030 Pharmacology
037 Drug Literature Index
039 Pharmacy
LA English
SL English
AB Objective and Design: This study examines the local and regional effects of exogenously administered interleukins 10 (IL-10) and 12 (IL-12) on pulmonary granulomas mediated by Th1/type 1-(IFN-.gamma.) and Th2/type 2-(IL-4, IL-5) cytokines. Materials and Treatments: Granulomas (GR) were induced in presensitized CBA mice by embolization of beads coated with Mycobacteria tubeurculosis or Schistosoma mansoni egg antigens. Before challenge, osmotic pumps distributing IL-10 or IL-12 (50 .mu.g/kg/day) were implanted intraperitoneally, then GR and draining lymph nodes were examined 4 days. Methods: GR sizes and composition were determined by morphometry and differential analysis. Isolated GR macrophages and draining lymph nodes were assessed for cytokine production by ELISA. Results: IL-10 did not effect GR sizes but reduced neutrophils in type 1 GR. IL-12 minimally reduced type 1 GR but decreased the type 2 lesion by up to 70%, primarily curtailing eosinophils. Type 2 GR macrophages were

unaffected but type 1 were impaired by IL-10. Conversely, type 1 GR macrophages were more resistant to IL-12 while type 2 showed enhanced IL-10, IL-12 and TNF, but reduced MCP-1 production. In lymph nodes, IL-10 caused paradoxical effects, enhancing IFN-.gamma. in the type 1 and decreasing Th2 cytokines in the type 2 response. Exogenous IL-12 profoundly augmented IFN-.gamma. and abrogated type 2 cytokines while inhibiting intrinsic IL-12 production in lymph nodes. Conclusion: These findings provide novel information regarding cytokine regulation and the effects of systemic cytokine therapy.

CT Medical Descriptors:
*inflammation
*lung granuloma
*lymphatic system
*macrophage function
animal cell
animal experiment
animal model
article
controlled study
drug effect
drug resistance
enzyme linked immunosorbent assay
eosinophil
female
intraperitoneal drug administration
lymph node
morphometrics
mouse
neutrophil
nonhuman
osmotic pump
schistosoma
slow release formulation
Drug Descriptors:
*recombinant interleukin 10: PR, pharmaceutics
*recombinant interleukin 10: PD, pharmacology
*recombinant interleukin 12: PR, pharmaceutics
*recombinant interleukin 12: PD, pharmacology
gamma interferon: EC, endogenous compound
interleukin 10: EC, endogenous compound
interleukin 12: EC, endogenous compound
interleukin 4: EC, endogenous compound
interleukin 5: EC, endogenous compound
macrophage chemotactic factor: EC, endogenous compound
mycobacterium antigen
tumor necrosis factor: EC, endogenous compound

L18 ANSWER 11 OF 12 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
AN 96261857 EMBASE
DN 1996261857
TI Gene therapy in pediatric oncology.
AU Benaim E.; Sorrentino B.P.
CS Division of Experimental Hematology, St Jude Children's Research Hospital,
332 N Lauderdale,Memphis, TN 38105-2794, United States
SO Investigational New Drugs, (1996) 14/1 (87-99).
ISSN: 0167-6997 CODEN: INNDDK

CY United States
DT Journal; General Review
FS 016 Cancer
022 Human Genetics
030 Pharmacology
037 Drug Literature Index
LA English
SL English
AB An increased understanding of the molecular mechanisms of cancer and the ability to introduce exogenous genes into mammalian cells has led to the development of oncologic treatment strategies based upon gene transfer. Preclinical animal models have suggested a variety of approaches which are now being tested in pediatric trials. Studies using marker genes to trace cell origin have already generated important information regarding autologous bone marrow transplantation for pediatric cancers. A variety of therapeutic genes are also being clinically tested. Trials are underway to determine if introduction of immunostimulatory genes into cancer cells can be used to enhance host antitumor immunity. Treatment of primary brain tumors with insertion of drug sensitization genes is a promising new therapy that is also being clinically evaluated. Other strategies such as insertion of drug resistance genes into hematopoietic cells, anti-oncogene therapy, and tumor suppressor gene replacement are being tested in adults and may find use in pediatric cancer treatment. Although gene transfer offers promising new approaches for the therapy of pediatric cancer, many technical problems remain which limit efficacy and widespread use. Further basic research in the molecular biology of cancer and in vector development will be required to realize the full potential of gene therapy strategies.
CT Medical Descriptors:
*childhood cancer: TH, therapy
*gene therapy
*gene transfer
acute granulocytic leukemia: TH, therapy
adenovirus
adolescent
antineoplastic activity
autologous bone marrow transplantation
brain tumor: TH, therapy
child
clinical trial
drug resistance
drug sensitization
expression vector
hematopoietic cell
hodgkin disease: TH, therapy
human
infant
major clinical study
marker gene
meta analysis

neuroblastoma: TH, therapy
preschool child
priority journal
review
school child
tumor immunity
tumor suppressor gene
virus vector
Drug Descriptors:
cancer vaccine: PD, pharmacology
cytokine: EC, endogenous compound
gamma interferon: PD, pharmacology
granulocyte colony stimulating factor: PD, pharmacology
granulocyte macrophage colony stimulating factor: PD, pharmacology
interleukin 2: PD, pharmacology
interleukin 4: PD, pharmacology
interleukin 7: PD, pharmacology
liposome
thymidine kinase: EC, endogenous compound
tumor necrosis factor alpha: PD, pharmacology

L18 ANSWER 12 OF 12 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
AN 94014069 EMBASE
DN 1994014069
TI Controlled release, biodegradable cytokine depots: A new approach in cancer vaccine design.
AU Golumbek P.T.; Azhari R.; Jaffee E.M.; Levitsky H.I.; Lazenby A.; Leong K.; Pardoll D.M.
CS Department of Oncology, Johns Hopkins Univ. Sch. of Medicine, 720 Rutland Avenue,Baltimore, MD 21205, United States
SO Cancer Research, (1993) 53/24 (5841-5844).
ISSN: 0008-5472 CODEN: CNREA8
CY United States
DT Journal; Article
FS 016 Cancer
022 Human Genetics
026 Immunology, Serology and Transplantation
037 Drug Literature Index
LA English
SL English
AB Experimental studies using murine tumor models have demonstrated that potent systemic immunity can be generated using tumor vaccines engineered by gene transfer to secrete certain cytokines. The underlying physiological principle behind these strategies involves the sustained release of high doses of cytokine at the site of the tumor. In some cases, this paracrine approach appears to enhance tumor antigen presentation and avoids systemic cytokine toxicity. The widespread clinical use of autologous cytokine gene transduced tumor vaccines may be limited by the technical difficulty and labor intensity of individualized gene transfer. We have therefore explored an alternate approach to generating sustained release of cytokines local to the tumor cells. High doses of granulocyte-macrophage colony-stimulating factor encapsulated in cell-sized gelatin-chondroitin sulfate **microspheres** were mixed with irradiated tumor cells prior to s.c. injection. This vaccination scheme resulted in systemic anti-tumor immune responses comparable to granulocyte-macrophage colony-stimulating factor gene transduced tumor

vaccines.
CT Medical Descriptors:
*malignant neoplastic disease
animal cell
article
biodegradation
controlled study
drug half life
female
gene transfer
genetic transduction
histology
immune response
mouse
nonhuman
priority journal
subcutaneous drug administration
tumor cell
vaccination
drug administration
drug dose
pharmacokinetics
sustained release preparation
Drug Descriptors:
microsphere
***cancer vaccine: AD, drug administration**
***cancer vaccine: DO, drug dose**
***cancer vaccine: PK, pharmacokinetics**
*granulocyte macrophage colony stimulating factor: AD, drug administration
*granulocyte macrophage colony stimulating factor: PK, pharmacokinetics
*granulocyte macrophage colony stimulating factor: DO, drug dose
chondroitin sulfate
cytokine: DO, drug dose
cytokine: AD, drug administration
cytokine: PK, pharmacokinetics
gamma interferon